Enhancement of Declarative Memory Performance Following a Daytime Nap Is Contingent on Strength of Initial Task Acquisition

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Study Objectives: In this study we examined the benefit of a daytime nap containing only NREM sleep on the performance of three declarative memory tasks: unrelated paired associates, maze learning, and the Rey-Osterrieth complex figure. Additionally, we explored the impact of factors related to task acquisition on sleep-related memory processing. To this end, we examined whether testing of paired associates during training leads to sleep-related enhancement of memory compared to simply learning the word pairs without test. We also examined whether strength of task acquisition modulates sleep-related processing for each of the three tasks.

Subjects and Procedure: Subjects (11 male, 22 female) arrived at 11:30, were trained on each of the declarative memory tasks at 12:15, and at 13:00 either took a nap or remained awake in the sleep lab. After the nap period, all subjects remained in the lab until retest at 16:00.

Results: Compared to subjects who stayed awake during the training-retest interval, subjects who took a NREM nap demonstrated enhanced performance for word pairs that were tested during training, but not for untested word pairs. For each of the three declarative memory tasks, we observed a sleep-dependent performance benefit only for subjects that most strongly acquired the tasks during the training session.

Conclusions: NREM sleep obtained during a daytime nap benefits declarative memory performance, with these benefits being intimately tied to how well subjects acquire the tasks and the way in which the information is acquired.

Keywords: Sleep, nap, declarative, memory, NREM sleep, slow wave sleep

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IT IS BECOMING INCREASINGLY CLEAR THAT NREM SLEEP, ESPECIALLY SLOW WAVE SLEEP (SWS), IS IMPORTANT FOR THE PROCESSING OF HIPPOCAMPUS-dependent declarative memories,[1-6] with SWS hypothesized to provide the optimal electrophysiological and biochemical state for this type of processing.[7,8] When sleep occurs in the form of a short daytime nap, it is very common to obtain only NREM sleep, without entering REM sleep, which would usually occur at least 90 minutes into the sleep period. The few studies examining the effect of daytime naps on memory have made use of this knowledge, demonstrating that daytime naps containing only NREM sleep (including SWS) facilitate verbal declarative memory (semantically related paired associates),[9] with one study showing that paired associates improvement is contingent on whether subjects obtained SWS during the nap.[10] These findings represent a first step forward in our understanding of how daytime naps benefit declarative memory processing. However, there are many questions still to be explored. To this end, the present study examines the benefits of a daytime NREM nap on a spectrum of declarative memory tasks, and begins to assess the importance of factors related to task acquisition and their potential to modulate sleep-related memory processing.

Disclosure Statement

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To more broadly assess the declarative memory benefits of NREM sleep obtained during a daytime nap, subjects were trained on 3 well-known declarative (hippocampus-dependent) memory tasks. The first task was an unrelated paired associates task, a more difficult counterpart to the commonly used related paired associates task.[3,4] The task comprises pairs of common words that lack an inherent semantic relationship (e.g., shirt–paper). Two nonverbal declarative memory tasks that do not rely strongly on previously learned concepts were also evaluated: the Rey-Osterrieth complex figure test (ROCFT; a measure of visuospatial declarative memory) and a maze learning task adapted from the task used by Brenda Milner on a large sample of hippocampal lesion patients including HM.[11] Both of these tasks are void of semantically charged landmarks, objects, or verbal material that would have been previously learned by subjects. To date, no studies have used this particular maze learning task, and only 2 have examined the effect of sleep on memory using the ROCFT. In epileptic patients it was shown that performance on the ROCFT correlated positively with low frequency EEG spectral power (<1.25 Hz) overnight,[12] and in schizophrenic patients the amount of SWS correlated positively with overnight ROCFT performance.[13]

In the present study we also explored the extent to which different methods of information encoding modulate the effect of sleep on memory. The impetus for exploring encoding factors was based on two studies by Smith, et al.[14,15] who found that only when rats successfully acquired an operant conditioning or passive avoidance task was there an increase in subsequent paradoxical sleep. These findings suggested for the first time that the extent of task acquisition may be an important modulator of the effect of sleep on memory processing. Support for this general finding comes from a recent PET study demonstrating that the strength of acquisition of a serial reaction time task

is correlated with increased brain activation (regional cerebral blood flow) during post-acquisition REM sleep.[16] Similarly, it was shown that stronger acquisition of a motor adaptation task not only correlates with an increase in slow wave activity (SWA) during subsequent sleep, but this increase in SWA is correlated with enhanced performance following sleep.[17] Given these findings, it becomes clear that the individual's success in acquiring a task may be an important factor in understanding how sleep facilitates memory formation.

In addition to the assessment of individual differences in acquisition, the level of task acquisition can be experimentally manipulated to assess the preferential effect of sleep for information that is more strongly acquired. A recent study by Schmidt et al.[18] has shown that not only does spindle density increase significantly during a daytime nap following the encoding of a difficult (but not an easy) paired associates task, but that this increase in spindle density correlates with improvement in paired associates recall.

To assess the importance of task acquisition in modulating sleep-related memory processing, we created 2 encoding conditions within the paired associates task. To date, almost all sleep-dependent consolidation studies have employed a "study-test" paradigm,[19] whereby subjects learn a list of word pairs, and then perform cued recall tests until a specified performance criterion is met (e.g., 60% correct or one perfect recall trial[2,3,20]). However, it is still unclear whether immediate testing leads to enhanced paired associates encoding, which in turn allows sleep to more strongly facilitate memory processing, or whether sleep imparts the same performance benefits to subjects that simply learn the word pairs without immediate testing. Interestingly, in a recent study that did not examine sleep/wake differences it was shown that when subjects were tested immediately after learning declarative information (a text passage), recall after one week was superior to recall of subjects that underwent multiple study sessions without being tested.[19] To add to our understanding of the nature of task acquisition and its potential to modulate the effects of sleep on memory, subjects in the present study were immediately tested on a subset of the word pairs during the training session (referred to as "tested" word pairs), while the remaining word pairs were studied without immediate test (referred to as "untested" word pairs).

In the present study, performance on all 3 declarative tasks was assessed following a 3.5-h training-retest interval that included a daytime NREM nap or no nap. To test the extent to which task acquisition factors modulate sleep-related memory processing, subjects were not only exposed to 2 modes of paired associates encoding, but for each task subjects were also divided post hoc into high and low performers based on training performance (i.e., those performing in the top and bottom half of the sample based on a median split). This allowed for an analysis of the effect of the subjects' ability to acquire each of the 3 tasks as well as the effect of 2 different modes of paired associates acquisition (tested vs. untested) on sleep-related memory processing.

METHODS

Subjects

A sample of 39 undergraduate students of diverse ethnic composition participated in the study. Six of the original 39 subjects were excluded from statistical analysis because they either did not obtain SWS (n = 3), they entered REM sleep (n = 2), or did not sleep during the nap period (n = 1). From the final sample of 33 subjects (11 males, 22 females, mean age = 23.3 y), 16 subjects were assigned to the nap condition and 17 to the no-nap condition. All subjects were medication free and abstained from caffeine and alcohol 24 h prior to participation. A sleep log was obtained from all subjects indicating bedtime, wake time, and total sleep time for the 3 nights prior to the study. All subjects were paid for their participation.

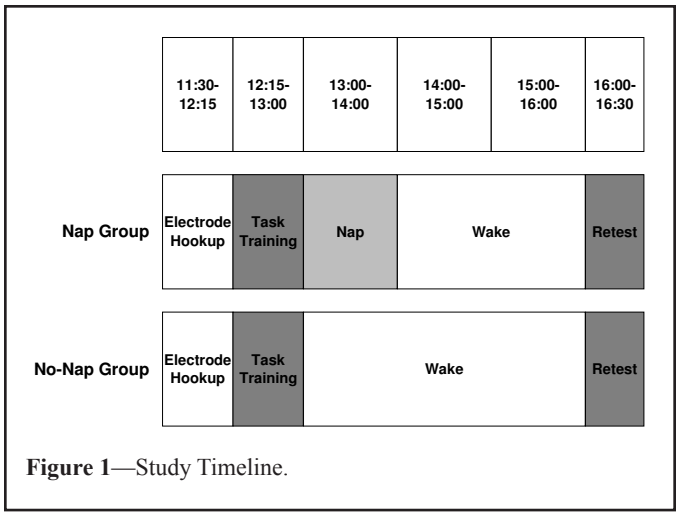

Figure 1—Study Timeline.

Procedure

Subjects arrived at the sleep laboratory at 11:30 (Figure 1). Between 11:30 and 12:00 subjects were shown the laboratory sleep chambers, signed the consent form, and completed a demographic information form. At 12:00, 9 electrodes were applied to record sleep, including central electroencephalography (EEG; C3-A2 and C4-A1), electro-oculography (EOG), and chin electromyography (EMG). To create similar experimental conditions, all subjects, including no-nap subjects, had the same 9 electrodes applied, and subjects were not informed of group assignment (nap or no-nap) until after the training session. Subjects trained on the 3 declarative memory tasks at a computer in sound-attenuated rooms from 12:15 to 12:45. The order of task presentation was fully counterbalanced across subjects. After the training session, subjects were assigned to the nap or no-nap group. At 13:00, nap subjects entered individual sleep chambers to take a nap. At the same time, no-nap subjects entered other sleep chambers and sat quietly for a period of 10 to 12 minutes, a time period comparable to that experienced by nap subjects prior to sleep onset. This condition was imposed primarily to address the issue of rehearsal of information that might occur with nap subjects prior to sleep onset. After this 10 to 12 min-period, no-nap subjects were taken to a separate room to watch a television program (e.g., an episode of Seinfeld) until nap subjects joined them at approximately 14:00. Nap subjects attempted to sleep for a period of approximately one hour. No subjects were awakened from SWS. After the sleep period, nap subjects joined the no-nap subjects to watch a movie until the retest session at 16:00. At 16:00, all subjects were retested on the same 3 tasks presented in the same order as during the training session.

Table 1—Sleep Parameters

	Minutes ± SEM	% of TST ± SEM
SL	14.97 ± 2.92	
TST	48.28 ± 3.49	
WASO	5.66 ± 2.33	
S1	4.78 ± 0.89	10.63 ± 1.96
S2	21.28 ± 1.61	46.19 ± 3.28
S3	14.13 ± 1.76	29.81 ± 2.84
S4	7.34 ± 2.77	13.36 ± 4.39
SWS (S3+S4)	21.47 ± 3.23	43.17 ± 4.03

Note. SL-latency to sleep onset (first epoch of sleep); TST-total sleep time; WASO-wake after sleep onset; S1-S4-stages 1-4; SWS-slow wave sleep

Sleep data for the nap group are presented in Table 1. Sleep log data revealed no differences between nap and no-nap subjects in amount of time awake prior to the study (P = 0.47), total sleep time the night before the study (P = 0.28), and average total sleep time for the 3 nights prior to the study, (P = 0.17) (Table 2).

Table 2—Pre-study Variables

	Nap	Wake	t_{31}	P
Wake prior to learning	4.9	4.6	0.74	0.47
TST night before study	7.1	7.6	1.1	0.28
Mean TST 3 nights prior to study	7.1	7.6	1.4	0.17

Note. Time was measured in hours; TST-total sleep time.

Tasks

Semantically Unrelated Paired Associates

Sixty word pairs were created from common objects (e.g., "alligator" and "cigar"), and were randomly paired to eliminate semantic relationships between the pairs. Subjects were instructed to visualize the 2 words interacting with each other, such that, in the case of "alligator–cigar" they might imagine an alligator smoking a cigar. Each word pair was presented serially for 2 seconds with a 100 ms interval between word pairs. All word pairs were presented in Times New Roman font (font size = 54). After presentation of all word pairs, subjects completed a cued recall test, during which they were presented the stimulus (first) word of 20 of the word pairs (randomly selected from the 60 presented pairs), and were asked to type the target word that completed the word pair. No feedback about whether each answer was correct or incorrect was given after subjects entered each response during the cued recall test. After completion of the 20 tested word pairs subjects viewed all 60 word pairs once more, this time presented each for one second, with a 100 ms interval. At retest subjects were shown, in random order, the stimulus words for all 60 word pairs, and were asked to recall as many of the target words as possible.

Maze Learning Task

The maze task is a computerized version of the "bolt head maze" used by Brenda Milner with the patient HM and a large sample of hippocampal lesion patients.[11] Our maze is a 13x13 array of squares, with each square representing either a correct step in the path of the maze, or a wall. Subjects start at the "start" button in the lower left hand corner and move left-right or up-down (but not diagonally) clicking each square with a mouse. If a subject is on the correct path, each square lights up green. If the subject hits a "wall" the square lights up orange. With each forward mouse click the preceding square returns to its original gray color. The first time through the maze subjects progress blindly from start to finish, but with each subsequent trial, subjects commit more of the path to memory. The maze program displays the time and the number of errors per trial. During the training session subjects completed 5 maze trials, recording on a response sheet the trial time and number of errors at the end of each trial. At retest subjects completed 8 maze trials. The number of maze trials at training and retest was based on a pilot study showing that 5 training trials produced substantial learning (subjects improved by approximately 38 errors from the first to last training trial) without reaching plateau, while 8 trials at retest allowed for a more exhaustive assessment of memory.

Rey-Osterrieth Complex Figure Test

The Rey-Osterrieth complex figure test (ROCFT) is a standard neuropsychological test used primarily as a clinical assessment tool to screen for brain injury that also measures visuospatial integration capacity and short-term visual memory. In this study subjects were presented the complex figure and were given 5 min to copy the entire figure onto a blank sheet of paper. If subjects finished copying the figure before the allotted time they were instructed to go over their work for the remainder of the time. At retest, subjects were again given 5 min to copy the figure from memory. Administration of the ROCFT differed from traditional methods in that recall was assessed approximately 3.5 h after the baseline session (instead of the usual 20-min interval), and all subjects were informed that that they would be retested on the figure later in the day. Scoring of the complex figure was based on a modified version of the Boston Qualitative Scoring System (BQSS),[21] such that the 6 configural elements, 9 clusters, and 6 details were given a 0, 0.5, or 1 point score. Zero was scored if less that half of the element was represented, or if orientation and position criteria were violated. A score of 0.5 was given if greater than 50% but less that 100% of the element was represented or if only orientation or position was violated. One point was given if 100% of the part was represented and orientation and position criteria were met. A total of 21 points could be obtained on this task.

RESULTS

Entire Sample

Unrelated Paired Associates

As expected, the number of tested word pairs recalled following the training session was similar for nap and no-nap subjects

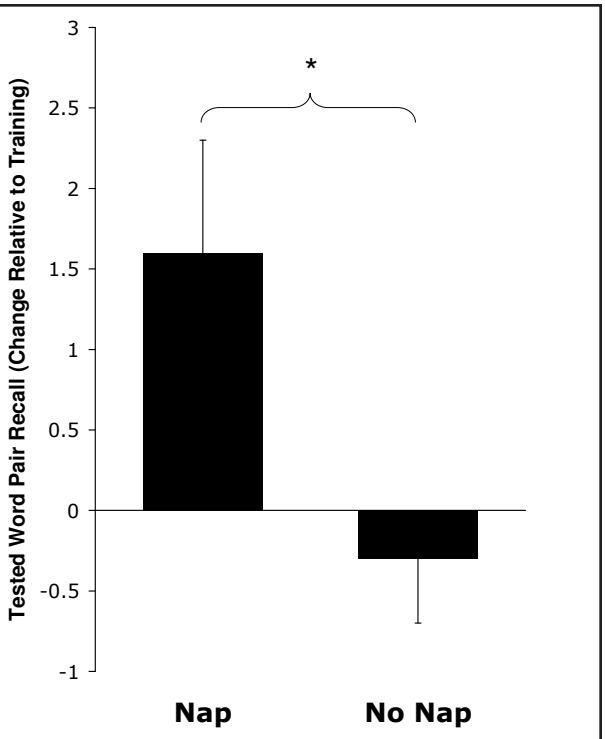

Figure 2—Tested paired associates performance, measured as change in recall at retest relative to training. Bars represent means ± SEMs. *P < 0.05.

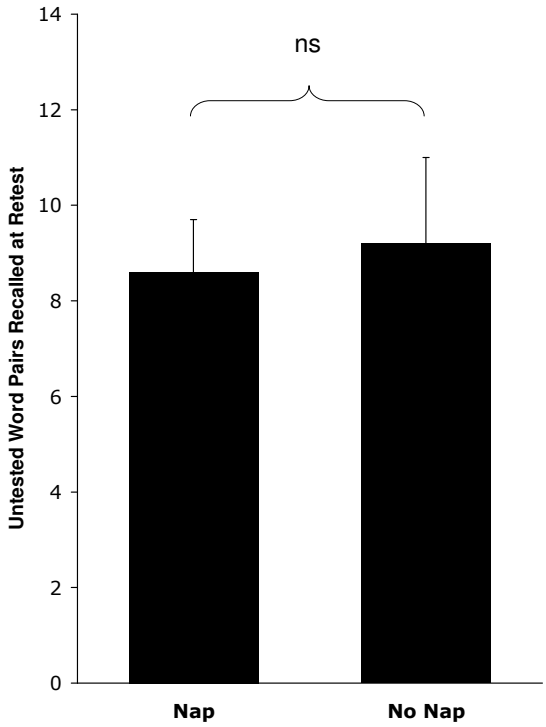

Figure 3—Untested paired associates performance. Note: Because the untested word pairs were not tested during training, only retest scores are presented. Bars represent means ± SEMs.

(nap group: 7.4 ± 0.8, no-nap group: 9.5 ± 1.3 (mean ± SEM, t_{31} = 1.31, P = 0.2). At retest, when high and low performing subjects were combined, recall of tested word pairs was shown to improve significantly from baseline training to retest for the nap group (+1.6 ± 0.7, t_{15} = 2.23, P = 0.04), and this recall enhancement was significantly greater than no-nap subjects, whose recall actually decreased compared to their baseline training performance (-0.3 ± 0.4; sleep group (nap vs. no-nap) by time (training vs. retest) interaction, $F_{1,31}$ = 5.26, P = 0.03) (Figure 2). For the 40 untested word pairs, the same 2x2 ANOVA could not be conducted, because subjects were not tested on these word pairs during training, only at retest. Therefore, we conducted an analysis of covariance, using training performance on the tested word pairs as a covariate, which revealed no difference in recall between nap and no-nap subjects at retest, (nap group: 8.6 ± 1.1, no-nap group: 9.2 ± 1.8, one-way ANCOVA, $F_{1,30}$ = 1.60, P >0.2) (Figure 3).

Maze Learning

The nap and no-nap group performed similarly during baseline training for number of errors committed per trial (nap group: 39.2 ± 5.3, no-nap group: 31.3 ± 4.3, t_{31} = 1.17, P >0.2) and average time to complete each trial (nap group: 103.0 ± 9.6 seconds, no-nap group: 90.9 ± 8.3 seconds, t_{31} = 0.96, P >0.3). Both groups improved significantly from training to retest for reduction in errors and for average time to complete each trial (all paired samples *t*-tests for the nap and no-nap group, P <0.001). When high and low performing subjects were combined, nap subjects demonstrated a nonsignificant 39% greater reduction in errors and a 33% greater reduction in time to complete the maze trials compared to no-nap subjects (error reduction: nap group: 16.8 ± 3.8, no-nap group: 12.1 ± 2.5, sleep group by time interaction $F_{1,31}$ = 1.13, P = 0.30; time improvement (seconds); nap group: 33.9 ± 7.1, no-nap group: 25.4 ± 5.4, sleep group by time interaction $F_{1,31}$ = 1.06, P = 0.31).

Complex Figure Test

During baseline training all subjects copied every detail (100%) of the complex figure within the 5-min time limit, except 3 who were excluded from this analysis. When high and low performers were combined, nap and no-nap subjects accurately recalled a similar number of complex figure elements (nap group: 14.8 ± 1.11, no-nap group: 13.7 ± 0.82; t_{28} = 0.75, P > 0.4).

Entire Sample Divided into High and Low Performers

Unrelated Paired Associates

The sample was divided into 2 groups: subjects that performed in the top half (high performers), and subjects performing in the bottom half (low performers) of the sample based on a median split of recall of the 20 tested word pairs during the training session. Within the group of high performers, nap subjects demonstrated enhanced recall of the tested word pairs compared their waking counterparts (nap group [n = 9]: 1.7 ± 1.0, no-nap group [n = 8]: -1.3 ± 0.6; sleep group by time interaction, $F_{1,15}$ = 5.66, P = 0.03; Figure 4a), while sleep had no facilitating effect on recall for subjects in the low performing group (nap group [n = 7], no-nap group [n = 9]; sleep group by time interaction, P >0.4). Within the high performing group the percentage of SWS obtained during the nap correlated positively with paired associates

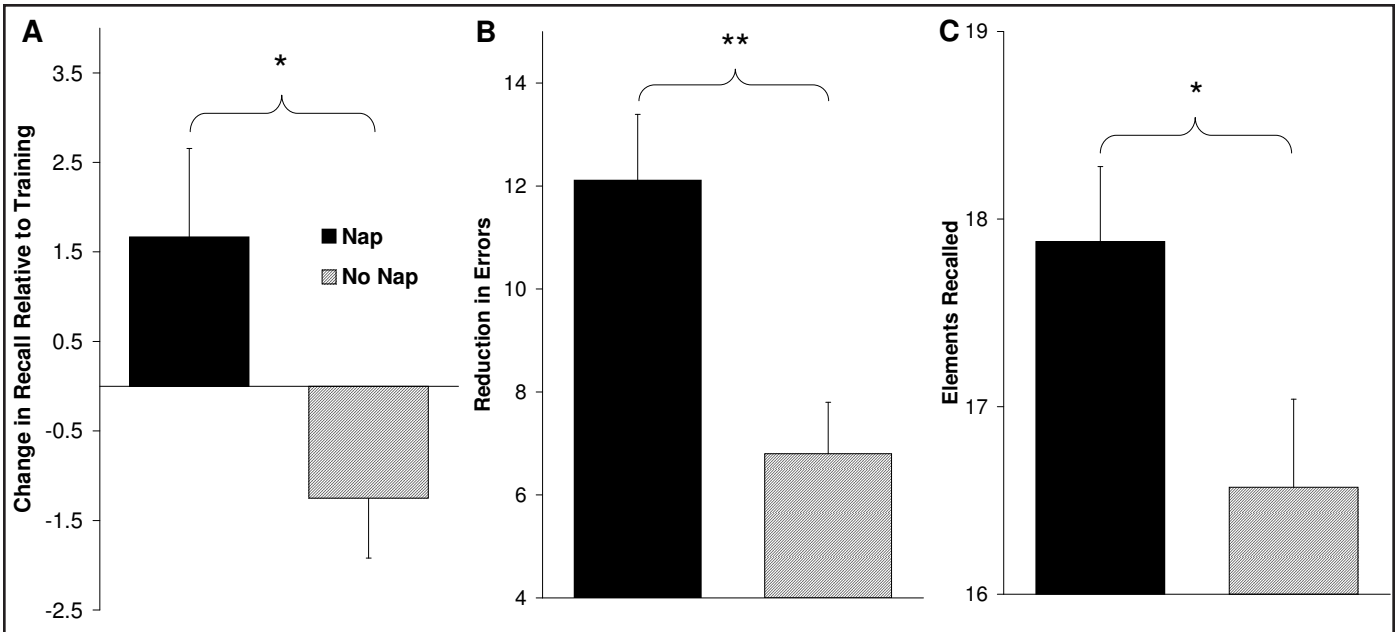

Figure 4—Performance across all three tasks for high performing nap and no-nap subjects. a) Paired associates performance measured as change in recall compared to initial learning. b) Maze learning performance measured as the reduction in errors compared to initial training. Note: higher values indicate a greater reduction in errors. c) Complex figure performance measured as the number of element recalled during the retest session. Bars represent means ± SEMs. *P < 0.05, **P < 0.01.

performance (r = 0.63, P = 0.06; Figure 5), while the correlation was negative for the low performers (r = -0.12).

Maze Learning

High performing nap subjects (i.e., subjects performing in the top half of the sample based on a median split for number of errors committed per trial during the training session) demonstrated greater improvement at retest than subjects in the high performing no-nap group for reduction in number of errors committed (nap group [n = 8]: 12.1 ± 1.3, no-nap group [n = 8]: 6.8 ± 1.0; sleep group by time interaction, $F_{1,14}$ = 10.81, P = 0.005; Figure 4b) and improvement in time to complete each trial (nap group [n = 8]: 22.4 ± 2.5, no-nap group [n = 8]: 11.8 ± 3.5; sleep group by time interaction, $F_{1,14}$ = 6.03, P <0.03). For the low performers (nap group [n = 8], no-nap group [n = 9]), sleep subjects did not improve more than their waking counterparts on both performance measures (sleep group by time interactions, P >0.5).

Complex Figure Test

When the sample was divided into high and low performers based on a median split of the number of elements recalled at retest, high performing nap subjects recalled significantly more of the complex figure than high performing no-nap subjects (nap group [n = 8]: 17.9 ± 0.40, no-nap group [n = 7]: 16.6 ± 0.47; t_{13} = 2.14, P = 0.05; Figure 4c). Recall in the low performing nap (n = 8) and no-nap group (n = 9) was similar, P >0.9.

Analysis of Task Specificity for Each High Performing Group

Sleep-related memory enhancement within high performing groups was task-specific (i.e., there was not a single group of high performing individuals demonstrating sleep-related enhancement across all 3 tasks). Independent samples *t*-test revealed that, while each group of high performers showed a clear sleep-related performance benefit for the specific task which they performed well on, these benefits did not transfer to the other 2 tasks (P >0.18 for all comparisons), except for high performers on the ROCFT who also showed a sleep-dependent performance on the paired associates task (P = 0.03).

DISCUSSION

Studies have shown that recall of semantically related word pairs (e.g., Clock-Hands) following a period of sleep is greater than when recall follows an equivalent period of wakefulness.[3,9] The present study extends this general finding by examining the benefit of a brief (~45 min) NREM-only daytime nap on unrelated paired associates performance. Consistent with previous studies that employ a study-test paradigm, we observed sleep-dependent enhancement of recall of the tested word pairs. In contrast to tested word pair performance, performance on the untested word pairs was similar between nap and no-nap subjects at retest. In response to this intriguing finding, we proffer the hypothesis that a test session immediately following the learning of this hippocampus-dependent task serves to more effectively prime relevant hippocampal and neocortical networks for subsequent sleep-dependent information processing.

While the neurophysiological mechanisms of underlying this sleep-dependent memory enhancement are not fully understood, theories of sleep-related memory consolidation clearly suggest that the electrophysiological and biochemical brain state produced during NREM sleep should be an optimal time for declarative memory consolidation.[7,8] Buzsaki suggests that a "hippocampo-neocortical dialog" occurs primarily during SWS to strengthen the memory trace, with the hippocampus generating

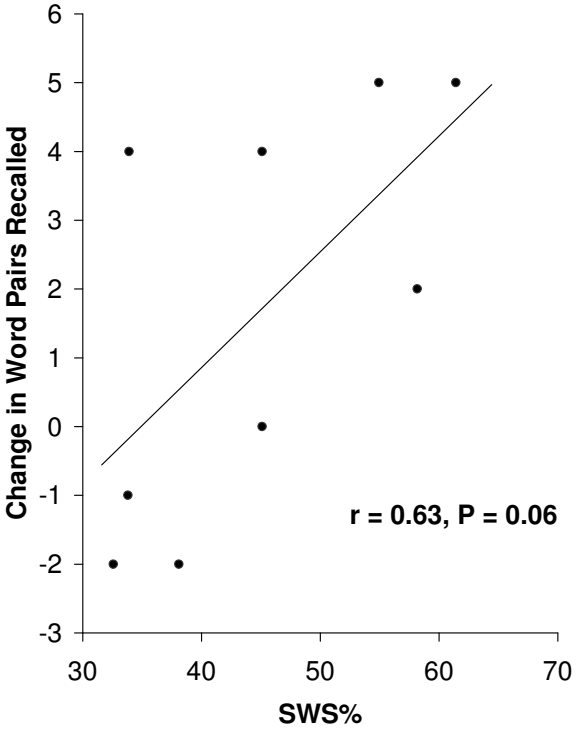

Figure 5—Correlation between percentage of SWS and change in recall of tested word pairs (relative to training) in the high performing nap group.

spontaneous sharp wave-ripple (SPW-R) complexes believed to provide efferent potentiation of cortical targets activated during information encoding.[22] Acetylcholine levels, which are at their lowest during SWS, have also been shown to be necessary for optimal declarative memory processing.[4,23]

Following from this physiological model of sleep-dependent memory consolidation, one implication of the study-test method would be that hippocampal and neocortical networks activated during presentation of the word pairs are reactivated during immediate recall during the training session, which better primes these networks for subsequent NREM sleep-related processing. Indeed, a number of imaging studies reveal that localized cortical regions (especially inferior prefrontal cortex) activated during the encoding of word stimuli[24,25] are reactivated during immediate retrieval,[26-28] possibly strengthening the initially activated cortical circuits. Conversely, if word pairs are untested, sleep-related facilitation of performance would not be expected, because relevant, learning-related hippocampal/neocortical networks would not have been adequately activated for subsequent sleep-related memory processing. While this notion remains speculative, it is concordant with the current findings, as well as existing hypotheses regarding the physiological basis of sleep-dependent memory processing.

Examining the sample as a whole, we found that the nap and no-nap group performed similarly on the nonverbal declarative memory tasks (ROCFT and maze learning), which was unexpected given the fact that declarative memory tasks have been shown consistently to benefit more after periods of NREM sleep compared to equivalent periods of wakefulness,[3,9,29] and that performance on declarative tasks has been correlated with SWS-related hippocampal activity.[5,6] However, one doesn't have to look far to see that this finding is clearly related to how well subjects performed the tasks during the training session. For each task, nap subjects that performed in the top half of the sample during training showed clear sleep-dependent performance benefits compared to their non-napping counterparts, whereas a similarity of performance was observed between nap and no-nap subjects in the low performing groups. One possible interpretation of this important finding is that subjects that demonstrate greater facility to learn each of the tasks are better equipped physiologically to benefit from sleep-related mnemonic processes. Indeed, strong positive associations are beginning to emerge between general measures of aptitude (e.g., Raven's Advanced Progressive Matrices and the Multidimensional Aptitude Battery) and sleep-related events such as stage 2 spindle count[30,31] and number of rapid eye movements.[30] In a related vein, two studies have shown that fast learning rats show increased REM sleep following successful acquisition of a shuttle avoidance task[14] and an operant conditioning task.[15] These findings suggest that there may be inherent physiological differences between subjects that may in part determine whether sleep will confer greater performance benefits.

It is relevant to note here that even though the beneficial effect of a daytime nap on paired associates recall was shown for the entire sample, when subjects were divided into high and low performers, as with the nonverbal declarative tasks, we found that the strength of this overall effect is also concentrated in the difference between high performing nap and no-nap subjects, while we found no difference in recall performance for the low performing nap and no-nap subjects. Not only do high performers benefit more from sleep than their non-napping counterparts, but this performance gain is correlated with percentage of SWS obtained during the nap, strengthening the general finding that SWS-related processes make a unique contribution to memory processing of verbal declarative memory tasks.

In summary, the present study demonstrates that a brief bout of NREM sleep (~45 min) obtained during a daytime nap facilitates memory processing for unrelated paired associates, and that this enhanced performance is tied to how the word pairs were learned (i.e., whether they were tested or untested during the training session). Results for all three declarative memory tasks demonstrate that sleep-dependent performance enhancement following a daytime nap depends on how well subjects acquire the tasks during the training session. We would suggest that the findings of the present study, in combination with findings from previous studies, begin to make a case that not only does sleep play a special role in memory processing, but that the benefits of sleep are clearly modulated (across multiple declarative memory tasks) by the strength with which information is initially acquired.

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