Interference Induces Improvement across Wake but not over Sleep in the Weather Prediction Task

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A Thesis in the Field of Biology

for the Degree of Master of Liberal Arts in Extension Studies

Harvard University

March 2011

Abstract

The ability to make predictions based on information extracted from patterns and frequencies of past events is a critical aspect of learning. This study investigates the effect of a nap on performance in a task that has been used as a measure of learning and memory of this type—the Weather Prediction Task (WPT). Here, two similar versions of the task are used to investigate the effects of interference after sleep and across wake.

In the WPT, subjects learn to associate presented card combinations with fictitious weather conditions of sun or rain, where each card has a specific probability of occurring with each weather condition. The essential probabilistic nature of the task is not revealed to the subjects. Yet, even when explicit knowledge of the problem is limited, subjects do improve on the task with training. Earlier work with the WPT has shown that an implicit memory route is activated as well during learning, so that effective performance on the task (and in probabilistic category learning in general) involves both implicit and explicit memory. One earlier study demonstrated improvement in performance based on original score on the WPT with sleep, suggesting that at least some memory consolidation occurs over a night of sleep. Here, improvement on the WPT was measured after a 90-minute nap with and without interference.

Interference training is thought to disrupt incompletely stabilized memories of a task through the application of additional training sufficiently similar as to use the same rules of memory consolidation as the original training, but which is also sufficiently different so as to be an effective competitor with the original learning scheme. This was expected

to impair retest scores on the original scheme for all subjects. But since sleep has been show to support off-line improvement, an only somewhat reduced effect of interference was expected in the subjects who slept compared to those who did not.

In this study, interference training with an alternate card set is administered at 2.5 hours after the first training session. For the sleep group subjects, this is immediately after a 90-minute nap. (Control subjects are awake for this period, and both groups are divided into interference and non-interference groups.) Based on data in earlier studies showing complete memory stabilization after six hours, interference is applied during that window in order to maximize the chance of seeing an interference effect.

As expected, subjects showed a trend toward improvement in performance after sleep without interference. With interference, however, a significant *improvement* was induced across wake as compared with sleep. This is contrary to expectations and provokes questions about the effects of interference. Since wake group subjects in particular showed improved performance on the Weather Prediction Task following interference training, it is possible that the effects of interference are not modulated by memory stabilization state alone.

Earlier work shows that sleep alters the quality of memory in the WPT. I have shown here that in a similar probabilistic task, sleep does not offer protection from the destructive effects of interference. Further, an unexpected benefit is seen with interference across wake in the WPT in observation mode that earlier work suggests may derive from a perturbation of implicit and explicit memory components of the task, though this remains a question, as does the mechanism for the differential effects of interference seen between sleep and wake.

Acknowledgments

I offer my appreciation to the study participants for all their efforts; my deepest gratitude to my thesis director, Dr. Robert Stickgold, for his support and guidance throughout the project; to Dr. Matthew Tucker for his essential training and advice; to thesis advisor Dr. James Morris for allowing this project to take shape. Thanks to Nam Nguyen for providing crucial administrative support and to Alex Morgan for offering her programming expertise.

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Chapter I

Introduction

Sleep has the capacity to influence what we remember (Ellenbogen, et al., 2009) and, without conscious effort, can even give us a subtly different understanding of an experience than we would have if we had simply been awake (Djonlagic, et al., 2009 Suppl,). Does this affect how we make decisions? The adage that sleeping on a problem can have an auspicious effect by morning has in it a kernel of awareness of the vague calculus that might be at work. In a growing effort to explore the biological effects of sleep, studies supporting the premise that memory consolidation processes are critically active during sleep have appeared at an accelerating rate (Stickgold & Walker, 2005). Research examining creative problem solving, for example, demonstrates an increase in that ability after a night of sleep (Cai, Mednick, Harrison, Kanady, & Mednick, 2009). And, historical anecdotes include more than one tale of a nineteenth-century chemist arriving at a solution to a critical problem only after some sleep. Kekulé's solution of the benzene structure came after a nap by the fire; Mendeleev's cards of the elements were said to have taken the published form of the periodic table after his sleeping on the problem gave him further insight into their periodicity (Stickgold & Ellenbogen, 2008; Trimble, 1981). What is happening in the sleeping brain that supports these kinds of insights? A relatively recent and growing line of research is actively seeking answers to questions surrounding experimental evidence that suggests we tend to solve problems differently after sleep.

Scientific studies investigating sleep and memory have put the question this general way: Do we forget less over a night of sleep (Stickgold, 2005; Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994)? The reasoning behind this was that if we do, then this could be simply due to the arrival of less input of competing information—or, interference—during sleep than would occur with the ordinarily broad range of sensory input we receive passively during the day. The preponderance of evidence is that something in fact actively changes in the sleeping brain that measurably alters memories of earlier learning in a way not seen across the day. A particularly fruitful line of research has found strong sleep-dependent effects in the reinforcement of non-declarative, procedural memory tasks in subjects who slept after training as compared with those who remained awake (Stickgold, 2005; Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002).

With tests of declarative memory—veridical recall of words in a list, for example—sleep effects exist as well, but the change is not straightforward. Experiments show that subjects who have slept are slightly better at veridical recall but are far better at identifying the underlying gist of a list of words than those who have stayed awake (R Stickgold, personal communication; Payne, et al., 2009). These investigations into the sleep-dependence of memory consolidation and fMRI studies following parallel lines of research now suggest differences in processing between wake and sleep groups. Results further illuminate the problem of *where* in the brain sleep effects in memory might be acting, giving weight to the argument that part of what sleep does is to work within the memory consolidation system, perhaps increasing the efficiency of some kinds of stored memories. And still, the latest work on this topic shows that this is a simplified view. Integrative stages beyond consolidation continue to process and reorganize declarative memories at a systems level, moving memories out of one system and into another, facilitating assimilation and abstraction, for example (Stickgold & Walker, 2007; Walker & Stickgold, 2010).

Sleep-dependent Consolidation in Procedural Tasks

The mechanism and path of memory consolidation in general and sleep-dependent memory consolidation in particular remains unknown. Yet, experiments probing the course of the consolidation process show that sleep effects on memory processing can be significant, ranging from the robust, increased performances found in some procedural memory tasks to a more subtle, nuanced understanding of a simple list or of a probabilistic or mathematical relationship. Most curious is that all of these changes occur in the sleeping brain without conscious thought—offline, as it were. With no deliberate effort on our part, sleep does appear to alter fundamentally the course a memory takes in its processing.

A relationship between sleep and memory consolidation was re-established in 1994, following earlier work, with a study on a visual perception skill in which improvement on performance at the task was observed overnight and was found to be associated with the presence of rapid eye movement (REM) sleep (Karni et al., 1994). More recent studies show evidence of sleep-dependent memory consolidation in a number of tasks in both the declarative and non-declarative memory domains (Stickgold, 2005; Stickgold & Walker, 2005). Among those papers exploring complex cognitive learning, a recent study shows sleep-dependent improvement in performance on the Weather Prediction Task (WPT), a probabilistic category learning task (Djonlagic et al., 2009). Since the WPT requires information integration across multiple cues and is generally considered to be non-declarative in nature (Ashby & Maddox, 2005), expectations at the outset of this study were that results of these tests would align most closely with other procedural memory tasks and exhibit increased performance after sleep.

Interference and Memory Stabilization

Memory stabilization is a measure of memory consolidation that classically answers the question how resistant is a memory to interference. In earlier studies, improvements seen in procedural skills in sleep subjects are reduced or eliminated when cross-training on a similar task is administered within six hours of the first training. (Stickgold & Walker, 2007). This is an example of the interference effect, an accepted indirect measure of memory stabilization. After six hours, current theory holds that a wake-mediated stabilization prevents interference from having an effect, and interference testing applied after that critical time should have little effect. In this study, we trained subjects in the WPT early in the day (in a method described in detail below) and applied interference training within this six-hour window with the expectation that interference effects should be seen.

Sleep-dependent memory consolidation may function by increasing the efficiency of memory retrieval and activation through brain plasticity (Stickgold & Walker, 2007). Test results show that different brain regions become active during retest depending on whether the subject has slept or not. Interpretations of these differences based on the known functions of the brain regions involved suggest that a night of sleep results in a reorganization of memory that allows more precise motor output, faster motor mapping of volition, improved sequencing of movement, and reduced demand on spatial monitoring and emotional burden (Walker & Stickgold, 2006). Taken together, these studies offer a glimpse of the degree of plasticity inherent in the memory consolidation process, and of the nature of the broad-based changes in processing that sleep must induce.

Still, the mechanism and timing of memory consolidation remains elusive: the fMRI images tell us something has changed after sleep, but these early investigations support only the broadest of interpretations, and they remain in some sense as shadows on the cave wall. Do these same changes hold for the probabilistic category learning of the WPT? It would be interesting to see the results of fMRI images with and without sleep in the WPT to look for any similar shift in locus of processing, but this method of testing is outside the scope of this study.

Sleep Stages

A positive correlation was found in an earlier study using the WPT between initial post-training performance on the task and the amount of REM sleep subjects had in the following night (Djonlagic, et al., 2009). This is of interest as it provides at least indirect evidence that sleep-dependent processes are at work in the memory processing associated with this task. This study’s protocol is designed to capture sleep stage information with the object of looking for any similar correlation between how subjects perform on the task and the amount of time spent in any sleep stage.

The canonical night's sleep is composed of a sequence of five 90-minute cycles during which the brain switches between discrete activity states: rapid eye movement (REM) sleep and the four stages of non-rapid eye movement (NREM) sleep, Stages 3 and 4 of which are the deepest, also known as slow wave sleep (SWS) (Stickgold, 2005). Sleep stage effects are seen by definition when learning in a sleep-dependent memory consolidation task is correlated with one or more sleep stages. This sleep stage dependence can be as varied as the tasks themselves: For example, sleep-dependent motor sequence skill learning (a finger tapping task) shows a strong Stage 2 NREM correlation in the fourth quarter of the night ($r = 0.72$, $p = 0.008$) (Walker et al., 2002). Visual procedural learning appears to show both a REM and SWS effect, with correlation in task improvement to early SWS and late REM periods; a motor adaptation task shows a SWS effect (Huber, R., et al., 2004). It is at this point unclear what drives the memory consolidation process to selectively reprocess information in one sleep stage or another, if this is what is happening. However, since subjects performing the WPT in an earlier study exhibited a REM sleep stage effect, the expectation was that we would find a similar correlation with REM sleep and learning in the WPT (Djonlagic et al., 2009).

An electrode montage commonly used in sleep studies was utilized in this study, including EEG, EMG, and EOG monitoring of brain waves, eye movements, and muscle tone during sleep and giving the information necessary to calculate the amount of time each of the sleep group subjects spent in the various sleep stages. Through data analysis, we report any correlation between sleep stage and learning on the task.

Nap Study

A significant improvement in retest scores after sleep in some training modes was seen in an earlier study using the WPT (Djonlagic, et al., 2009). We use a nap study protocol here to ask first whether we find similar performance effects with a 90-minute nap as were seen over a full night of sleep. In addition, we introduce interference as described earlier. The nap study is a well-established method of gathering information on sleep states that is certainly more efficient than studying the data of a full night of sleep but which serves a significant role of its own in sleep research. Two possible confounds exist in reports of memory consolidation over a full night of sleep. First, there is the circadian question.

Might any memory effect we see be modulated perhaps by circadian phase? The brain modulates a wide range of body rhythms that fluctuate over the course of the day, including cyclical temperature and hormonal levels that may impinge on memory in some unknown way. Another way of asking this question is, do subjects simply do better in the morning than in the evening on the task?

Also, there is the question of the permissiveness of sleep itself. Could sleep, in other words, somehow support the consolidation of memory passively, by shielding the mind from interfering activity, perhaps? The nap study addresses both questions. By training and testing all groups at the same time of day, one may eliminate any circadian confound. And, in the present nap study, the between-group difference in time awake is limited. Those taking a nap are awake for 3.5 hours during their time at the lab while the wake group is awake for 5 hours. However, a three-fold difference exists in overnight studies where the wake group spends 12 hours awake compared with 4 hours of wake time for the sleep group. By allowing as much as a 90-minute nap, we are hopeful that at least one complete sleep cycle (and all sleep stages) will be represented, and the chance of capturing any active sleep stage effect will be maximized. By allowing *only* as much as a

90-minute nap, any possible passive effects of sleep as a permissive environment for consolidation is minimized.

Mednick, Nakayama, and Stickgold (2003) addressed the power of a nap in memory consolidation, with the result that 'a nap is as good as a night' of sleep. Measuring sleep-dependent consolidation effects during a single sleep-cycle, 90-minute nap in a visual discrimination task, they found that a nap with both SWS and REM sleep stages functioned as well as a full night of sleep: same-day nap-dependent performance improvement was seen in the task at similar levels seen after a full night. In the nap study, if REM was missing from the nap, sleep-dependent memory consolidation was not observed. (All groups in that study had SWS—the nature of its contribution is unclear.) These results augur well for the use of a nap paradigm with the WPT in studying sleep-dependent memory consolidation.

Weather Prediction Task

Protocol in Brief. In the Weather Prediction Task (WPT), four cards with line drawings of simple objects serve as the stimulus elements. Subjects see one, two, or three cards at each trial and use these presentations to predict “sun” or “rain” weather conditions. Each card has a fixed probability of determining a weather condition, and the probabilities associated with the two- and three-card combinations are the sum of the individual card probabilities, but subjects are not informed of this.

At 11:30AM, subjects sit at a computer workstation and select a key for “sun” and “rain.” They are asked to attend carefully to the card combinations as they are presented. All subjects first encounter 200 training trials. Training in the WPT is by the observational mode. That is, for each training trial, subjects are presented with a card combination and, simultaneously, a picture of either a sun or a rain cloud. They mimic the weather condition displayed with a key press of either of their “sun” or “rain” keys while viewing the corresponding card combination. Immediately after these 200 training trials are completed, an on-screen message announces the start of the testing phase, which consists of 100 additional trials. In testing, however, there is no weather-indicating figure accompanying the card presentations, and subjects must respond with a “sun” or “rain” key based on their sense of what each card combination predicts.

Subjects are randomly assigned to one of four groups: Wake; Wake with interference; Nap; Nap with interference. At noon, the two nap groups begin a 90-minute nap monitored by EEG, while the wake groups watch videos in rooms nearby.

Interference in the WPT is applied at 2:00 PM to the two interference groups only. The no-interference groups watch videos during this time. Interference testing and training is procedurally identical the original set of trials—200 training trials in observation mode followed by 100 testing trials—except that the images on this card set are different. The interference card set is matched for line density and figure type with the original set, but the figures on the cards are changed.

At 4:30 PM, all subjects participate in a retest. For the retest, subjects see the identical 100 training trials as in the morning session, in which they are again asked to respond with “sun” or “rain” based only on presentations of cards. The original card set is used.

The optimal response on the WPT is the weather type most likely to appear with any particular given card combination. Performance on the task is the percentage of optimal responses in a given test session.

Rationale. The problem subjects face is that no combination of cards predicts the "weather" with 100% accuracy, since there is a *probabilistic* relationship to the outcome, with some cards better at predicting a particular weather state than others. As a result, the relationship between card pattern and weather remains elusive to subjects. Yet, some unconscious insight must occur, as subjects typically improve from chance to a near optimal score on the WPT after 350 trials (Ashby & Maddox, 2005). Debriefing comments from early studies using the WPT show that subjects are not able to verbalize well the probabilistic nature of the exercise, and analysis of subject responses shows that self-reported strategies of solving the WPT are unreliable: subjects improve in the task without being able to report accurately how they have completed it. (Gluck, Shohamy, & Myers, 2002). This result is consistent with the accepted classification of the WPT as an information-integration task that is expected to rely to a strong degree on implicit memory processes, but not exclusively so (Ashby & Maddox, 2005).

Subtle shifts in the modality of the training routine have a profound effect on post-sleep improvement on the WPT. If subjects are asked to first choose a weather outcome with a presented card set before being shown the outcome (feedback mode), there is far less skill enhancement after sleep seen than has been is seen in the observation mode, where subjects are shown the weather outcome during the training sessions. These variations in the training modality can account for as much as a 12% difference in post-sleep skill enhancement in the WPT (Djonlagic et al., 2009). For this study, I used the observation mode for its greater likelihood of reproducing a strong sleep-dependent effect than other training modalities. At the same time, it is recognized that the use of the observational mode in training likely increases the explicit memory component of the task. This is an important consideration, as the test has within it both implicit and explicit components, and as these in theory compete during memory processing (Zeithamova & Maddox, 2006).

A comparison of the 11:30 AM and 4:30 PM tests on the WPT for the sleep and wake groups without interference allow us to see firstly whether there is a comparable improvement in performance with a 90-minute nap as was seen earlier across a night of sleep. Secondly, by introducing a block of interference training and testing at 2:00 PM for half of the nap and wake subjects, one may ask whether a nap after learning successfully protects against interference. This is to say, does exposure to an alternative version of the WPT at 2.5 hours after learning the original version change performance at the end of 5 hours? Is there a difference between sleep and wake groups with interference? In general, one would expect a deleterious effect from interference, but any reduced effect of interference after sleep will be interesting; if there is no loss of improvement after sleep followed by interference, as this would show that sleep confers protection upon the memory acquired in the first training session.

Finally, the nap is monitored with EEG in order to obtain data on sleep stages and to ask whether any differences seen depend on the kind of sleep obtained.

Implicit vs. Explicit Memory

A sleep stage dependency or sleep-dependent skill improvement once identified for a task may depend on subtle and unobvious experimental factors. For the serial reaction time test (SRTT), simply telling the subjects in advance the nature of the test they will be taking appears to change the memory task from one of implicit to explicit memory, obliterating the sleep consolidation effect (Robertson, et al., 2004). The authors of a paper on probabilistic motor sequence learning point to a likely confounding of results when a high degree of explicit learning is present (Song, Howard, & Howard, 2007). In their study, no sleep effects were found.

These results are consonant with the model of dual memory systems known as the competition between verbal and implicit systems model (COVIS). In this model, explicit memory is mediated by a hypothesis-testing system of logical reasoning, while implicit memory is facilitated by a procedural learning system (Zeithamova & Maddox, 2006). Both systems attempt to solve learning problems simultaneously, but they are differentially weighted depending on the task at hand.

Sleep-dependent consolidation as has been observed in procedural memory tasks is a robust effect, but the possibility of improvement on the skill during wake on the one hand or a confounding implicit/explicit memory switch on the other both demand careful attention to controls and training protocol to account for or limit these effects.

There is considerable debate on whether the WPT should be considered rather more rule-based than information-integrating, depending on the mental strategy subjects might choose to use used for its completion (Ashby & Maddox, 2005). Yet, a strong post-training REM correlation was found with performance at initial testing in subjects who were trained on the WPT in observational mode (Djonlagic et al., 2010). I predict that the task will exhibit similar skill enhancement over a 90-minute nap as had been seen overnight, and a REM correlation with initial performance is anticipated. Cross-training interference is expected to reduce this effect, demonstrating incomplete stabilization.

Differences in any interference effect between nap and wake groups could provide additional, indirect evidence of memory stabilization.

Performance Strategy Shift

Following a classical conditioning model of implicit learning, subjects' performance in the WPT is expected to show gradual improvement with increasing numbers of trials (Gluck et al., 2002). Since subjects remain unaware of the probabilistic nature of the task, a better probe of strategy used for its completion than subjective reports is found in mathematical analyses of the subjects' responses. Such analyses have previously revealed that there is a shift in strategy for most subjects from a focus on single-card patters in the early trials to a more sophisticated strategy later, in which multi-card patterns are predicted with greater success (Gluck et al., 2002). This shift—can we call it insight with implicit learning?—is the key to achieving higher scores on the WPT. It is possible that the off-line enhancement found after sleep operates by facilitating the unconscious realization of the probabilistic nature of the task and an efficient transformation toward a multi-card strategy.

Subjects' own post-retest estimates of card probabilities offer some evidence that a change has occurred after sleep, but this too depends on training modality. In one study, subjects using the observational and short feedback training modes dichotomized the cards into two with equally low probabilities of sun and two with equally high probabilities of sun. In contrast, sleep subjects more accurately identified the actual probabilities. For these feedback modes at least, it appears from this evidence that subjects have acquired a more nuanced knowledge of the task after sleep. In the same study, but with the feedback training mode, subjects in both the wake and sleep groups tended to dichotomize the cards at retest. There was also little post-sleep improvement found in the feedback mode (Djonlagic, et al., 2009). This distinction among training groups clouds the theoretical picture somewhat, but serves at the least to point to a subtlety present here: different training modes likely provide different fractions of implicit and explicit memory in the route to learning.

Functional Shift in Learning and Memory

There appears to be a shift in brain region activity at some point around trial 50 in the WPT in normal subjects using the feedback mode (Ashby & Ell, 2001). fMRI studies show that at about this point, high activity in the medial temporal lobes begins to deactivate. At the same time, activity in the basal ganglia increases (Ashby & Ell, 2001; Ashby & Maddox, 2005). Is this the end point of memory integration in the WPT? Could sleep-dependent consolidation be directed at facilitating the transformation of activity from the medial temporal to a more basal gangliar route? Does this shift represent a trace of the unconscious insight that comes with experience in the WPT, and with sleep?

The present study was not designed to answer such questions, but rather, to ask simply, do we see in a nap similar evidence of memory consolidation and stabilization as were seen in a full night of sleep with the WPT? And, how are those changes affected by interference? As it turns out, our findings do bear on these larger, and perhaps more interesting, questions.

Chapter II

Materials and Methods

Subjects

Subjects were 40 healthy college age students (mean age = 20.9±2.0 years, range = 18-27 years) who have signed an IRB-approved informed consent form and who reported a normal sleep schedule (mean sleep duration = 7.3±1.0 hours for the three days prior to testing; sleep duration range = 5-9 hours for the two nights prior to testing). The subject population was limited to students enrolled at Boston University. Subjects who reported histories of drug abuse (including alcohol and narcotics), psychiatric or neurologic disorders, sleep disorders, or use of psychoactive drugs, sedatives, or hypnotics were excluded from the study, as were subjects who reported consuming >600mg/day of caffeine.

Procedure

I scheduled subjects to arrive at the Center for Sleep and Cognition at least three days after my initial communication by phone or email in which they indicated to me their intent to participate. Upon scheduling, they received via email a URL to a secure HIPAA-compliant online sleep log using Survey Gizmo and were asked to complete the log on each of the three mornings before their arrival. On the day of the study, participants arrived at 10:30AM, signed informed consent, and sat at separate Macintosh workstations to answer three computerized questionnaires: one general questionnaire to ensure compliance with the prerequisites, and the Epworth and Sanford Sleepiness Scales to establish measures of vigilance.

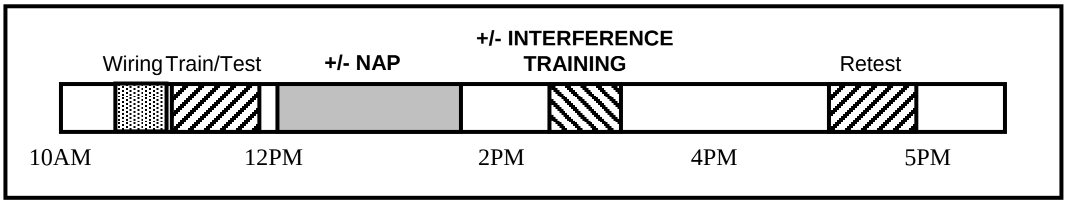


Figure 1. Study Protocol. A monitored 90-minute nap begins at 12 noon for Sleep groups. The AM training and testing and the PM retest at 5 h use Card Set 1; Interference training and testing at 2.5 h use Card Set 2.

At 10:45AM, all subjects were shown to research study bedrooms and prepared for polysomnograph (PSG) recordings of electroencephalography (EEG). Electrode application took place in the bedrooms that would be occupied later by the nap group participants, in part to accustom them to the sleeping environment. For each subject, after measuring and marking the cranium for electrode placement, the scalp was cleaned at the electrode attachment points with NuPrep (Weaver & Co., Aurora CO) and eleven conductant-filled electrodes were applied using EC2 electrode cream (Grass Technologies, West Warwick RI) on gauze (PSG montage: C3-A2, C4-A1, F3-F4, O3-O4, EMG, EOG), making no distinction between nap or wake groups. At 11:30AM, subjects returned to their original computer workstations to perform the initial training phase, which they did with PSG leads gathered behind their head, and carrying the 1.5 lb PSG connector box. At the computers, subjects were addressed briefly on the mechanics of the task. They first would chose the two keys on the computer keyboard they will use to signify each of the two weather conditions, “sun,” and “rain.” These keys retained their significance throughout the testing day. On their screens, the first of the testing program slides was visible, including instructions and with a set of four cards displayed. I asked subjects at this point to attend to the on-screen instructions and to observe the card images carefully when they were presented to them. The on-screen instructions were as follows:

“Welcome to the Weather Prediction Parlor. In this learning game you are the weather forecaster. You will learn how to predict rain or shine using a deck of four cards (the four cards are displayed, as in Figure 2):

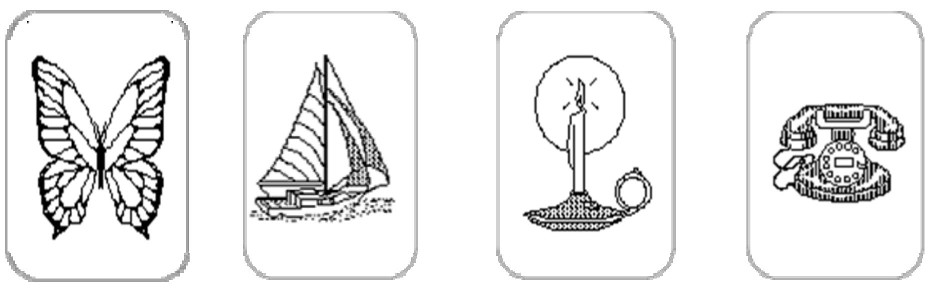


Figure 2. Card set 1. Initial slide display.

“For each day you will see between 1 and 3 cards and the weather they predict. Your job is to learn which cards predict Sunshine and which cards predict Rain. When you are finished looking at each set of cards, press the key for the weather it predicts to continue. Good luck!”

Observational Training

In 200 training trials, subjects saw displays of one, two, or three cards presented at 5-second intervals. Above the card display was a graphic image of the weather those cards predict, as well as the question, “Rain or Sun?” In this *observational* mode of training, the actual weather outcome was given. Subjects used their “rain” and “sun” keys to mimic the weather seen on screen–if the rain cloud appeared, they pressed the “rain” key. If the sun appeared, they pressed the “sun” key (See Figure 3). If no key were pressed, the reminder, “Answer now,” appeared on-screen after two seconds. After five seconds, the program moved on to the next trial regardless of whether an answer had been recorded. Faster responses did not advance the tempo of the training.

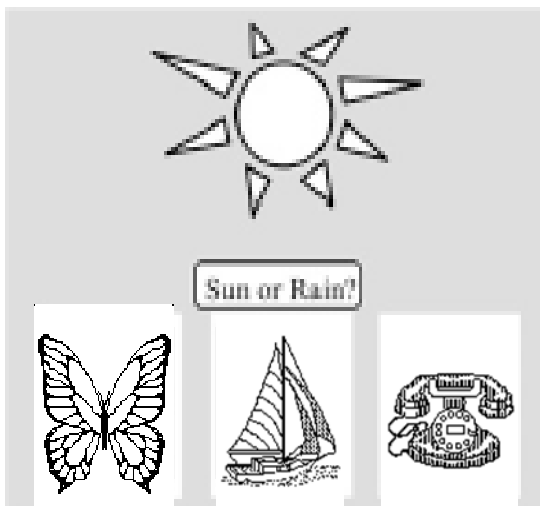


Figure 3. Training trial. Example.

First Testing Phase

Immediately following the training phase, an on-screen prompt let participants know that the testing phase had begun. In it, they were to answer with their best guess of “sun” or “rain” when prompted with presentations of the figure card combinations alone–no weather condition is displayed for these 100 trials, which were presented in 5-second intervals as in the preceding test trials (See Figure 4).

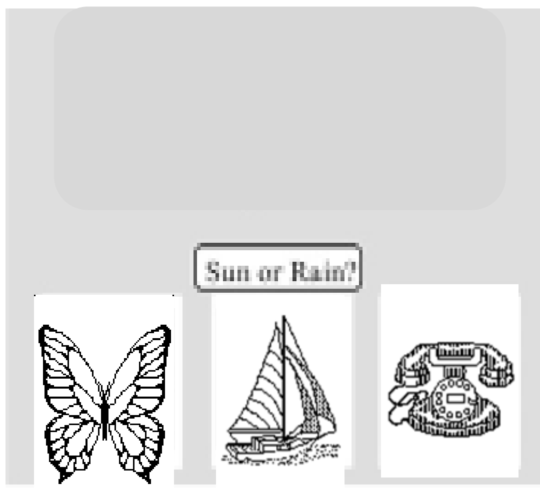


Figure 4. Testing trial. Example.

In both training and testing phases, fourteen of the sixteen possible card combinations (excepting the zero- and four-card combinations) were balanced across fifty-trial blocks, both by specific combination and by sequence. For example, the Butterfly-Boat pair appeared just as often in the first quartile as in the last, and just as often as Boat-Butterfly. The figures in this card set, deliberately chosen to represent distinct categories of objects, were also matched for density of line.

The probability of a positive (Sun) or negative (Rain) outcome for each card was fixed, as in earlier versions of the WPT, such that each card had probabilistic associations with the two weather outcomes as follows: Card 1: 24% Sun/76% Rain; Card 2: 42%

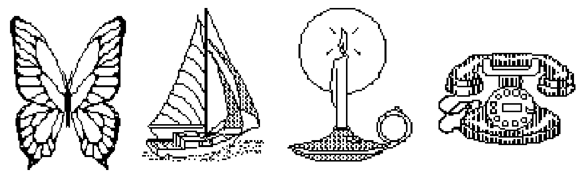
Sun/58% Rain; Card 3: 58% Sun/42% Rain; Card 4: 76% Sun/24% Rain. (See Figure 4) The correct subject response was the choice of the most likely weather outcome for any given card combination. That is, the outcome which had the largest probability. Yet, these values were unknown to the subjects.

Assignment to Wake and Sleep Groups

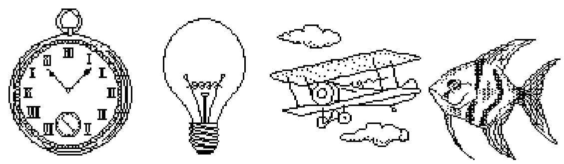
After initial training and testing, subjects were randomly assigned to one of four groups: 1. Wake/ No interference. 2. Wake/ Interference. 3. Sleep/ No interference. 4. Sleep/ Interference. At 12:00 Noon, subjects in the sleep groups were shown to private research study bedrooms. I explained that they had the opportunity for a 90-minute nap and when they were comfortably in bed, the PSG connector box was attached to the recording apparatus. The sleep subjects were told that they would next hear instructions through a speaker in the room and the lights are extinguished. I was able to monitor subjects by sound, video, and PSG. The bedrooms were insulated against light infiltration, and a white-noise device masked sounds from an active hallway nearby.

From an adjacent monitoring station, we began recording EEG signals using Grass EEG monitoring software. Subjects were then asked to blink five times, look to left and to the right, and finally to relax and try to sleep. I informed them that they would be awakened after 90 minutes.

Card Set 1. Initial training and testing; Retest (at 5 h).



% Sun:	24	42	58	76
% Rain:	76	58	42	24



Card Set 2. Interference training and testing (at 2.5 h).

Figure 5. Card sets with associated probabilities. Training and testing on card set 2 after the 90 minute sleep or wake period is designed as interference to the skill acquired during initial training and testing on card set 1. Both sets share probabilistic rules and are balanced across sets by object type and order of display.

Also at noon, subjects in the wake groups were shown to similar rooms and their EEG leads were removed. They were informed that they would not be taking a nap and were instructed to remain awake until called for the next test session. Wake subjects watched light comedy of their choice from a selection of DVDs while the sleep subjects slept.

Sleep subjects were awakened from their nap at about 1:30 PM, slightly later if they had only just entered REM sleep at about 90 minutes. I used the bedroom speaker to wake them, then entered the room to turn on the room lights and disconnect the PSG monitoring cable. The PSG leads were removed at this time.

Interference Training and Testing

At 2:00 PM, I assembled those subjects in the interference groups at the computer terminals for training and testing in the alternate card set 2 (See Figure 4). Two different card sets were used in this study, both adhering to the same probabilistic rules. Card set 1 was used by all subjects at initial training and testing and would be used in the retest at the end of the day. Card set 2 was reserved for use only by the two groups of subjects who received interference training and testing. Interference subjects experienced 200 trials of observational training with card set 2 followed immediately by 100 testing trials. Interference training and testing is identical in every respect with the earlier administration of the first card set with the exception of the images on the cards.

Between 2:30 PM and 4:30 PM, all subjects had the opportunity to eat a light meal in a cafeteria within the building after which they returned to chairs in the bedrooms to watch a selection of DVDs with a light, comic content.

Retest

At 4:30 PM, all subjects returned to the computer terminals for the final testing session of the day. As this test was most properly a retest of the morning's test, card set 1 was used with a 100-trial testing sequence. There was no training session.

Upon completion of the retest, subjects again provided ratings on the Epworth and Sanford Sleepiness Scales and filled out an exit questionnaire which asked broadly about their explicit strategy they used in the task, and also about their percentage estimate of the weather probabilities of the four cards—eight, if they were in an interference group.

Subjects lastly filled out payment request forms and left the center at about 5:00 PM.

Chapter III

Results

Through subject responses to our online sleep log, we found that subjects slept an average of 7.4±0.2 hours per night for the three nights prior to coming in to the lab, with a range of 5-9 hours. 86% reported 7 or 8 hours of sleep. This is consistent with the self-reported sleep periods of the pre-testing questionnaire, in which subjects reported a mean of 7.3±0.2 hours per night on the night before testing. The online form asked for detail on any sleep abnormalities, and 88% reported a normal night's sleep the night before their arrival. Those abnormalities listed were in general reports about the heat (it was summer), noises, or dreams during the night—nothing that would disqualify them from testing. 65% fell asleep within 30 minutes of turning out the lights.

In the exit questionnaire, we gathered data on napping habits as well as information on the subjects' explicit strategies for completing the task. However, only 12 subjects were asked to complete the section on strategies. Reported here are the napping data: 43% reported napping regularly, with a mean duration of 51.0±7.0 min per nap. Those who did nap did so on average 2.3±0.4 times per week.

In data from the sleepiness scales on the questionnaire, subjects reported that at 10:30 AM their mean subjective sleepiness was 2.5±0.12 on the Sanford Sleepiness Scale (SSS). This represents a degree of sleepiness between 2.0 and 3.0:

> 2 = Functioning at high levels but not peak; able to concentrate.
> 3 = Awake but relaxed; responsive but not fully alert.

At the end of the test day, at about 5:00 PM, the reported mean subjective sleepiness for all subjects was 2.2±0.16 (See Table 1).

Questionnaire responses from all groups:			
	Age	Hours asleep	
Mean (± sem)	20.9±0.3 years	7.3±0.16 hours	
Range	18-27 years	5-9 hours	
Nap reports	Naps per week	Nap Duration	
Mean	2.3±0.4 naps	51.0±7.0 min	
Range	0-7 naps	40-120 min	
Subjective alertness reports:			
10:30 AM	Concentration	Refreshed	SSS
Mean	71.3±3.1%	62.2±3.7%	2.5±0.12
Range	59.5-100	46-100	1-4
5:00 PM	Concentration	Refreshed	SSS
Mean	70.8±3.1%	67.2±3.1%	2.2±0.16
Range	30-100	31-100	1-5

5:00 PM Subjective alertness reports by group:			
	Concentration	Refreshed	SSS
All Nap subjects	73.0±5.6%	71.4±16.5%	2.2±0.73
Nap/No Interference	77.4±14.7%	72.7±5.5%	2.3±0.36
Nap/Interference	65.9±6.7%	68.4±6.0%	2.2±0.13
All Wake subjects	71.5±16.2%	64.2±18.6%	2.2±1.1
Wake/No Interference	77.1±4.6%	66.8±7.0%	1.9±0.30
Wake/Interference	64.8±6.5%	61.5±6.7%	2.5±0.46

Table 1. Questionnaire results. Sleep and nap log; subjective alertness reports; Sanford Sleepiness Scale (SSS).

There was no significant difference in subject-reported alertness or sleepiness between groups at 5:00 PM (See Table 1). Note that while the numeric difference in SSS between the Wake/Interference and Wake/No Interference groups in the 5:00PM response is apparently large, even these groups are not in fact statistically different for this measure (two-sample t-test, p=0.29).

Early in data analysis, it was observed that some subjects did not perform well in the initial, observational training. This was a serious concern, as we could not be confident that their subsequent testing scores would be meaningful. In observational training, subjects simply match the on-screen weather condition—a picture of a sun or rain cloud—with their key for sun or rain on the keyboard. This should be 100%, as the answer is given to subjects with each training trial. Allowing for a possible attention lapse or key-press error, scores below 95.0% do not represent trouble with the task *per se*, but rather indicate that a subject is simply not doing the task as described. We therefore excluded training scores lower than 95.0% from the study. By doing so, 10 subjects were excluded from the original 40. One further subject was withdrawn when it was discovered that an erroneous version of the final retest was administered. In each of the following calculations, N = 29 and the experimental groups are: Sleep/No Interference, N=8; Sleep/Interference, N=8; Wake/No Interference, N=8; Wake/Interference, N=5.

An analysis of the PSG sleep recordings was performed for all subjects, looking at the amount and proportion of nap time spent in each sleep stage. A few individual subject analyses were striking. For example, the subject who had the greatest score improvement also had the largest proportion of REM sleep in the nap. However, after performing the appropriate ANOVA tests and regression analyses, no correlation by group between successful learning of the task and sleep stage was found.

As per Djonlagic et al. (2010), scoring for all WPT training and testing trials is the raw performance adjusted for chance, and is given by Adjusted score = (raw score – 0.5)/0.5 Change in score on retest = Adjusted score$_{(Retest)}$ – Adjusted score$_{(Test1)}$

= 2 x (Raw score$_{[Retest]}$ – Raw score $_{[Test\ 1]}$)

Adjusted scores were calculated by 50-trial block in each training and testing for each of the subjects. We were concerned, on initial examination, that some subjects appeared to be performing well below chance on these measures (<19 of 50 correct, $p<.05$).

Subjects could have performed a total of fourteen training and testing blocks of 50. In examining representative response strings from each of the 50-trial blocks, we found that subjects were responding appropriately to changing weather cues but had effectively reversed their responses for long strings of trials, apparently confusing the sun and Rain keys. To correct for this apparent systematic error, we applied the general formula (%correct training block A = max(%training block A,100-training block A) to each of the possible 14 50-trial blocks in the data set, effectively fixing any inverted values. The corrected data from these subjects were used in all subsequent analyses.

When the simple numerical increase in percent correct score was calculated for the four groups, an unexpected increase in score in the Wake/Interference group was observed, as well as a puzzling absence of any improvement in the Sleep/Interference and Wake/No Interference groups (See Figure 6). While numerical increases are seen in the Sleep/No interference and Wake/Interference groups, no group showed statistical improvement or statistical difference from one another ($0.15< p >0.23$).

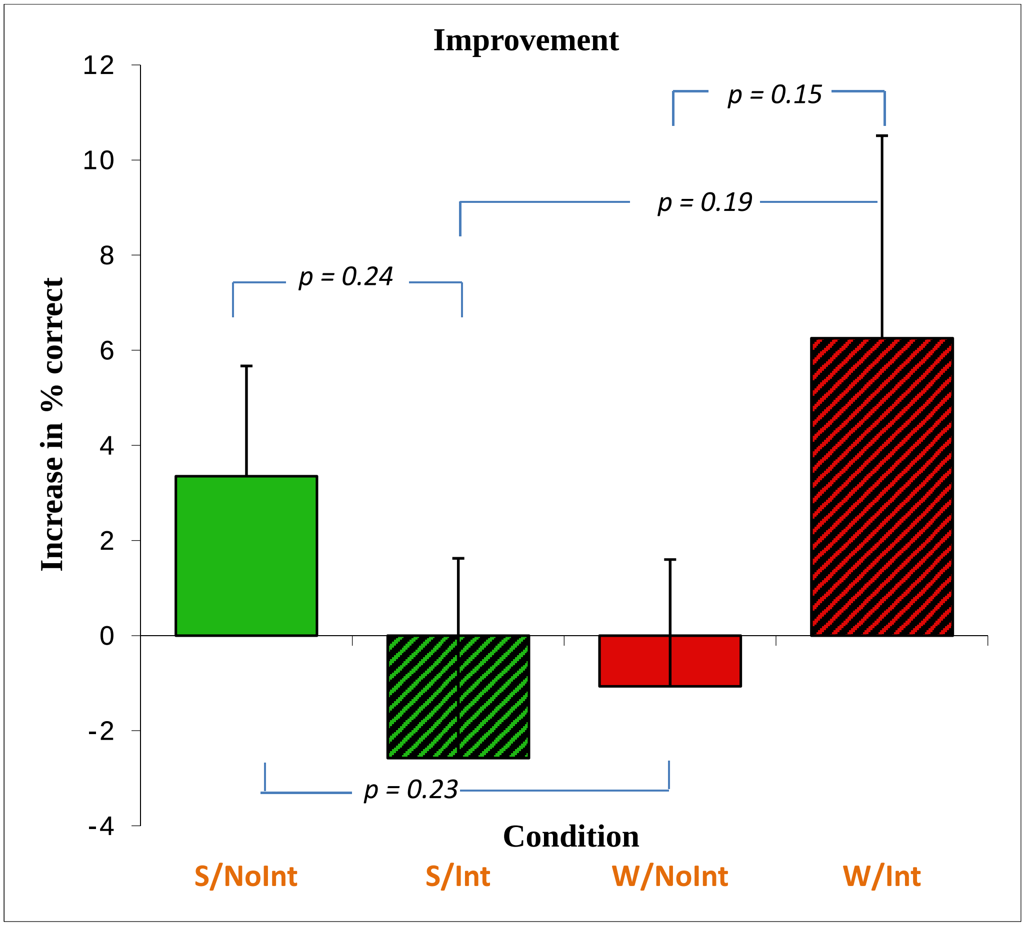


Figure 6. Improvement by group. 5 h improvement between post-training performance and retest with and without interference. (for all sleep *vs*. wake, $p = 0.70$) **S** = sleep; 90-min. nap ; **W** = wake. Neither sleep or wake, nor the presence or absence of interference training alone significantly changed performance.

In order to explore further the lack of 5 hour improvement in two of the groups, the Sleep/Interference + Wake/No Interference groups were paired for analysis. In the graph describing that pairing, the data begin to show signs of an interaction between interference and sleep, with R=0.90 in percent improvement *vs.* original test score (See Figure 7).

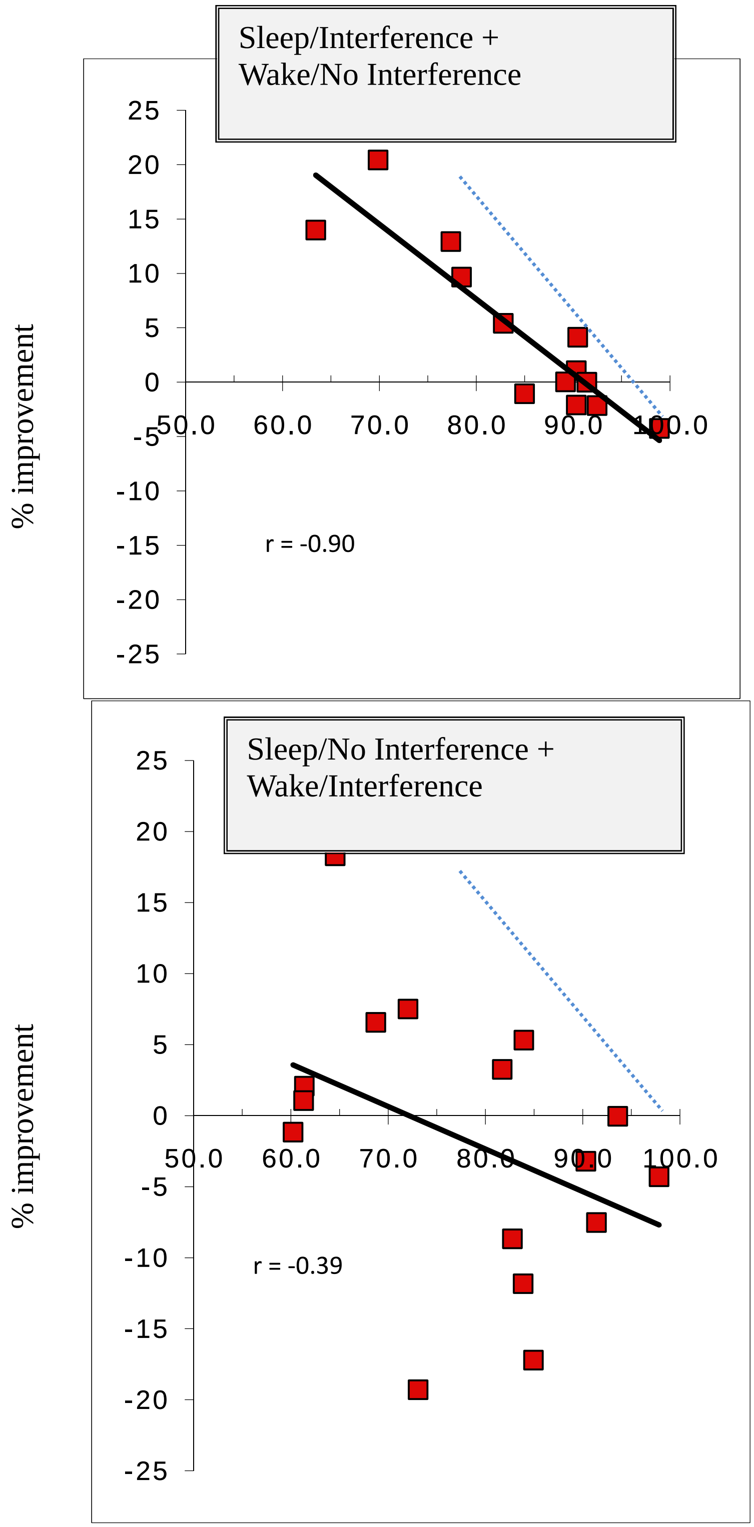


Figure 7. Group interactions emerge
when viewed as % improvement *vs*. original test score.
Dashed line is ceiling limit of possible improvement.

Indeed, by regressing improvement in test score against original score for the No interference groups, one sees by this measure a significant improvement after napping in the Sleep group (p=.005). In the Interference groups, it was the Wake group that exhibited significant improvement (p=.005). In contrast, the other two groups showed no significant improvement (both p values >.15 for the regression).

A 2 x 2 ANOVA was performed comparing percent score improvement at retest and found no significant difference between the Wake/Sleep groups or the Interference/No Interference groups. There was no hint of a main effect (p>.50 for both). However, the interaction *between* the groups achieved near significance (p=.065). This is to say, by these calculations, near significance is found in the differential impact of interference on percent score improvement in Sleep and Wake.

Based on this information, and with the knowledge that initial test score has an impact on performance, an additional ANOVA was run, adding initial test score as a covariate. Here, too, neither the Wake/Sleep groups nor the Interference/No Interference groups showed a main effect (both p values>.15), but the interaction between the groups is now significant at p=0.003. Initial test score also was found to predict improvement (p=.001) and we are at this point able to claim a highly significant, differential impact of interference on both Sleep and Wake groups. *Post hoc* tests comparing improvement between the two interference groups and with original test score as a covariate show a significant difference in 5 hr improvement between the two groups (p=.018). Without original test score as a covariate, however, this significance vanishes (simple t-test, p=.19).

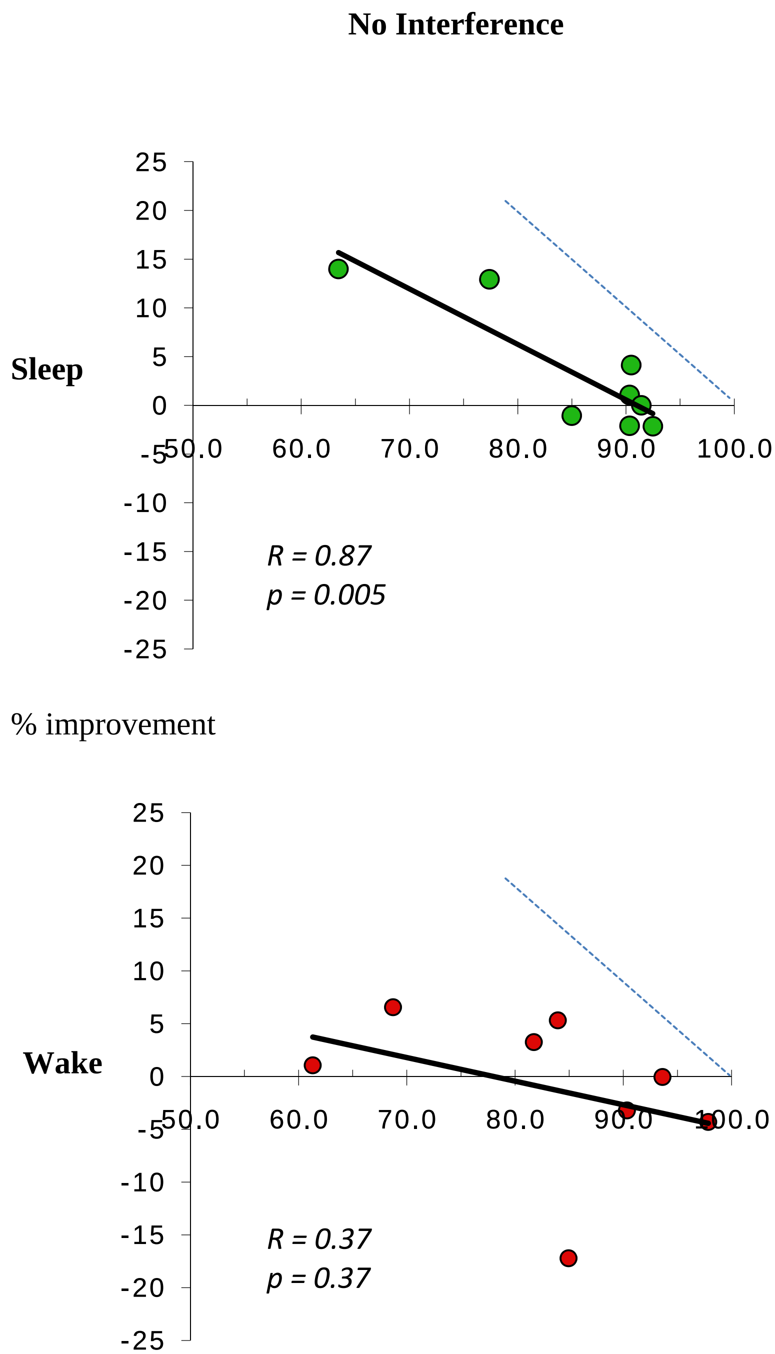


Figure 8a. No-interference regression plots. Percent retest improvement is plotted against initial post-training test performance. See score improvement with sleep. Dashed line is ceiling limit of possible improvement.

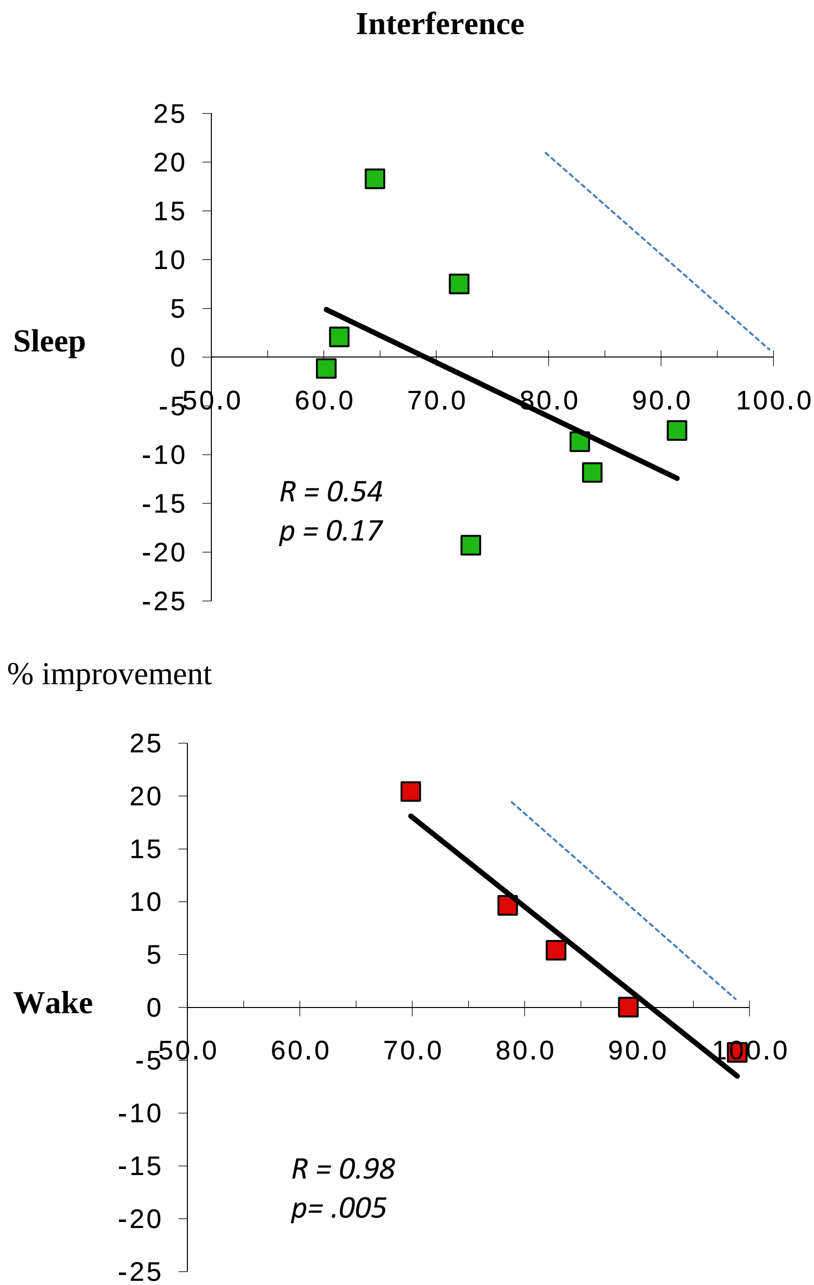


Figure 8b. Interference regression plots. Percent retest improvement is plotted against initial post-training test performance. See score improvement with wake. Dashed line is ceiling limit of possible improvement.

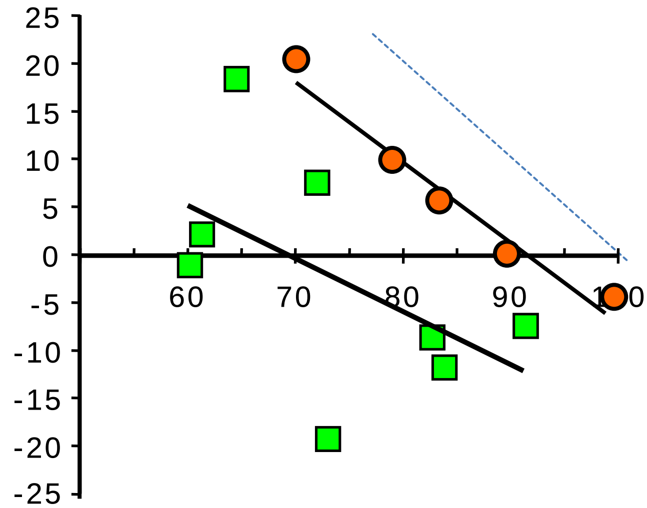


Figure 9. Interference regression plots, combined: Percent retest improvement is plotted against initial post-training test performance; squares: Sleep/Interference group; circles: Wake/Interference group. Dashed line is ceiling limit of possible improvement.

In Figure 9, percent retest improvement is plotted against initial post-training test performance for both Interference groups, revealing that for a given initial test performance, subjects in the Wake/Interference group are performing better than in the Sleep/Interference group. *Post hoc* analyses with initial test score as a covariate show significantly less improvement in the interference condition than the No-interference condition for Sleep groups ($p=.016$) and, again unexpectedly, a trend toward significantly more improvement in the Interference condition for the Wake group ($p=.081$).

Chapter IV

Discussion

Performance on the WPT should increase after a nap, based on results seen earlier in an overnight study (Djonlagic, et al., 2009). And interference, it was thought, should broadly reduce performance in both sleep and wake groups, but perhaps to a different degree in each owing to a difference in the state of consolidation achieved in the two conditions. I further expected to find a REM sleep correlation with either initial performance or degree of learning on the WPT, based on earlier results.

Given these expectations, the scores as measured after retest were at first glance disappointing. It was immediately clear that there would be no significant increase in performance to report for the nap groups. In fact, no significant change was seen in score for any group or for the Wake/Sleep or Interference/No interference pairings. The sleep group changes in numerical test score on retest were to some degree as expected by absolute difference, however, with a somewhat reduced performance in the Sleep/Interference group from the Sleep/No interference group, but these differences, too, fell short of achieving statistical significance.

That the highest retest scores were found in the Wake/Interference group was perplexing. How could interference induce better performance? This question would surface again with further analysis, but at this point the issue vanishes with the failure of statistical significance—there are no real differences to report by numerical retest score alone as a measure.

Looking again at the data in Figure 6, it seemed odd that the pairing of Sleep/Interference and Wake/No Interference should have similar values and that neither should have seen in increase in score improvement. It was this peculiarity that led to the pairing of those groups for analysis. The graph in Figure 7 hinted that the result of this effort may be fruitful. Notice in particular the Sleep/Interference and the Wake/No Interference groups together, graphed by percent improvement *vs.* original test score. One sees here a very strong R=0.90 for the grouping. Conversely, the Sleep/No interference and the Wake/Interference groups taken together by the same measure show a weak interaction at R=0.39. What this reveals is not clear, though, since both the sleep/wake and interference/no interference conditions vary, but from this we strongly suspected that there may be a genuine effect at play between sleep and interference in the WPT.

Earlier work with the WPT and sleep found that the extent of overnight improvement depends on the level of performance achieved during training, and that significant correlations were shown to exist between post-training test scores and improvement in sleep groups (Djonlagic, et al., 2010). This means that subjects with lower initial scores showed predictably more improvement at final testing than those who scored higher at initial testing. I had assumed that a similar relationship would exist for this nap study, and therefore the data were analyzed comparing percent retest improvement with initial post-training test performance for each group (See Figures 8a and 8b). The negative slope of the best-fit line for each group shows that we have reproduced the direction of the trend, though only two of these regressions achieve significance.

It is worth looking at these regressions more closely. Exactly those two groups that when graphed together in Figure 7 gave a strong R-value in the pairing also show significant correlations in Figure 8a and 8b as separate groups. Indeed, both the Sleep/No interference and the Wake/Interference groups show significant correlation and a more robust improvement when percent retest improvement is plotted against initial post-training test performance (both at p=0.005). Comparing both Wake group regressions, it is clear that Wake subjects with interference do better than Wake subjects without interference. Also from Figures 8a and b, Sleep subjects with interference tend to do somewhat worse than Wake subjects without interference.

Figure 9 combines the two Interference groups on one graph. In it, it is easy to see that subjects in the Wake/Interference group performed better than those in the Sleep/Interference group.

A curious shift occurred when the group data were analyzed not simply by change in performance but by adding original test score as a covariate. It was only at this point that significant, underlying group effects could be seen—both in the effect of sleep and of interference in the WPT. A *post hoc* analysis revealed that in the end a significant group effect did exist with the application of interference, but not the expected one. I found that interference effects improvement in the WPT differently depending on whether or not subjects had slept, with an unexpected increase in performance in the Wake/Interference group. The non-interference groups replicated with a nap the results seen earlier with a full night of sleep, showing better performance after a nap than an equal time awake.

Earlier studies suggest that the observation mode of training in the WPT utilizes a more explicit memory route—memory systems supported by activity in the MTL and prefrontal cortex—hippocampal-neocortical networks. This is in contrast to other training modes, which are more implicit in nature and would be supported memory systems in the striatum, which should see reduced activity in observational learning (Djonlagic, et al., 2010). Could this be the neural basis for the memory enhancement we see evidence of in the no-interference sleep group? Only with the benefit of additional studies including fMRI as a tool of comparison, however, can this question be answered definitively, and this is beyond the scope of the present study.

I had expected interference, of course, to interfere (with the retrieval of extant memories, with memory processing) but I have shown here that it doesn't do so uniformly. In fact, the data from the Wake/Interference group show an unexpectedly enhanced performance relative to all groups (See Figures 8a and 8b). There is a significantly increased performance relative to the Sleep/Interference group, which itself is reduced in performance from the Wake/No interference group, as expected.

Why is this? A study on the serial reaction time task (SRTT) touches on this point, if obliquely. In this sequence-learning task, it was found that the motor skill portion of the SRTT improved over wake with interference (Brown and Robinson, 2007). In these experiments, a word list was memorized after initial skill acquisition. Learning the list reduced significantly the subjects' ability to explicitly recall the sequence of the SRTT, while at the same time they were able to perform the motor skill portion of the task about 30% better than a group who had done a vowel counting exercise as a control. Their interpretation is that the declarative (explicit) component of the task was disrupted by the interference task, allowing off-line procedural (implicit) skill enhancements to take place (Brown and Robinson, 2007). One might also say of their experiment that the off-line implicit memory enhancement ordinarily seen after sleep was unexpectedly observed in this case during wake, unmasked by interference.

With this evidence, and in the context of my finding that the WPT response to interference can vary, in observation mode, depending on the presence or absence of sleep, I appear to have described a distinct example of an unexpected, differential effect of interference. That is, the use of the more explicit observation mode of learning in the WPT may have allowed, in wake, a similar induction of offline enhancement by interference in this study as was seen in the wake study using the SRTT. By the reasoning presented in the SRTT study, the exposure to an additional quotient of explicit memory features in the WPT task by the interference training groups in this study may have disrupted the explicit component of the learned memory, thus allowing off-line processing to occur via the competing, implicit memory system.

But, what of the sleep condition? There is a significant difference between sleep and wake among the interference groups (See Figure 9). Previous evidence suggests that after sleep, memory undergoes a qualitative change; subjects who slept after the WPT in observational and short feedback modes in an earlier study tended to describe more accurately the individual probabilities of the WPT cards in an exit questionnaire than those who remained awake, as if they had a more nuanced understanding of the probabilistic nature of the task. The wake group, on the other hand, grouped the four cards differently. They tended to dichotomize their response, correctly grouping those that tended to predict sun and those that tended to predict rain, but lacking the subtlety of the sleep group response, rating, for example, the strong and weak predictors of rain equally (Djonlagic, et al., 2010, Suppl.).

What is it about the quality of memory that has changed after sleep? And how does this change impinge on interference training? One may make the primary assumption that since I have effectively replicated—in a nap—the effect of post-sleep enhancement seen earlier in an overnight study with observational training in the WPT, the data do represent the effects of a similarly active sleep-dependent process. I hypothesize that the differences we see in the effects of interference with and without sleep are related in some degree to an interaction with those same or similar sleep-dependent memory processes. If this is so, one can argue that the changes in the quality of memory after sleep with the WPT in observation mode allow the known negative effects of (destructive) interference, but "protect" against the (constructive) positive effects of interference training described here.

Interference training in the WPT in observation mode clearly does not function as simply more learning: the Sleep/Interference group improved less with interference, as expected. Yet, interference training does not simply "confuse" the subjects: across wake, I found in an unexpected result that there could be a benefit from interference training. To fully explore the results of this study, it will be necessary to revisit the concept of interference and to test predictions about possible differential effects of interference across wake and after sleep. Possible probes for interference effect include the altered timing of interference to explore the memory stabilization state boundary, and the administering of interference tests in various training modalities (both observational and short feedback, for example) to explore the influence of the implicit-explicit quotient. Further, it would be interesting to see whether by subtly altering either the task itself, or, even the instructions which subjects are given, whether a constructive-destructive interference shift might be induced. fMRI studies should provide evidence on whether differences in processing exists in interference training after wake or sleep, and whether these differences persist on retest for either condition.

The present study was limited in sample size. The N of 5 for the Wake/Interference group is a serious limitation and the study should ideally be repeated with larger numbers.

With sleep, unconscious, off-line memory processes can alter our perception of a problem of a probabilistic nature and may bring us toward a more nuanced understanding of those problems. Earlier work suggests that memory reactivation and reprocessing may be integral to these changes. I have shown here that in a similar probabilistic task, sleep does not offer protection from the destructive effects of interference when applied before the window of memory stabilization has closed, suggesting the possibility that memory for the task is still labile after sleep.

I have also described an unexpected benefit from interference across wake, in which subjects who received interference training after a similar period of wake improved in performance significantly. If performance had merely not declined, the accepted assumption would be that memory for the task had become stabilized across wake. With this unexpected finding of a performance increase, however, it may be that stabilization state alone is not sufficient to predict the effects of interference.

It is not unreasonable to assume, based on earlier work by others, that constructive interference is induced when the subtle balance between implicit and explicit memory components of a task is perturbed to favor explicit memory processing. It is not obvious why interference training that is weighted toward explicit processing and does produce constructive interference across wake should have a differential effect that is dependent on sleep state or why sleep should protect against constructive interference. These questions remain unexplored.

Interference is widely used as a simple test of memory stability, in which a memory susceptible to the deleterious effects of interference is taken to be in an unstable state and a memory resistant to interference is seen as stable. Considering the possibility that additional differential interference effects may exist, and that these may depend on a balance of implicit and explicit memory types as well as sleep state, the argument for memory stability in the absence of an observable interference effect becomes less clear. In light of the data presented here, a more finely attuned approach to interference testing than has been customary may be necessary—one that accounts for these additional factors.

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