The ERP Old-New Effect: A Useful Indicator in Studying the Effects of Sleep on Memory Retrieval Processes

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Study Objectives: To verify that the classic "Old/New" memory effect can be detected after a long delay, and to investigate the differential influence of declarative memory processes after normal sleep and daytime wake.

Design: The protocol is a variation of a more traditional study-recognition test used in event-related potential (ERP) studies in which sleep or wake is inserted between the learning and recognition session in order to verify the existence of the Old/New effect (ie, positive shift that occurs when stimuli are repeated). ERPs were recorded during the recognition-test session. The protocol was based on early work that compared the effect of sleep on memory without recording sleep.

Setting: Data collection occurred in the outpatient sleep laboratory.

Patients or Participants: Results from 13 subjects (6 men) aged between 21 and 39 years.

Measurements and Results: The subjects performed the recognition memory test after sleep and daytime wake periods. More-accurate performance for the old (studied) stimuli occurred after the sleep session. Analysis of variance on correctly answered reaction times revealed a significant effect of condition (old/new) with no difference across session. A repeated-measure analysis revealed differences in "Old/New" effect, whereby the amplitude difference between the old and new items was larger after sleep than after wake.

Conclusions: This effect of sleep was found in early frontal and later posterior ERP components, processes that represent strategic, contextual processing and facilitation of episodic memory. Memory representation was not different across sessions. These findings suggest that sleep and wake facilitate 2 components of memory unequally, ie, episodic recognition and memory representation functioning.

Keywords: Declarative, episodic, memory ERP, sleep, memory processes

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INTRODUCTION

THE POSITION THAT SLEEP MAY PLAY A ROLE IN THE PROCESS OF MEMORY FORMATION DATES BACK TO THE REPORT OF JENKINS AND DALLENBACH IN 1924, claiming that recall performance improves following an intervening period of sleep.[1] Early studies showed that sleep can have an important role in memory retrieval.[2-4] However, research has resulted in mixed and contradictory conclusions.[5,6] This lack of agreement between studies may be a consequence of the differences in task characteristics[7,8] or the type of stimuli used,[6] likely addressing different subtypes of memory.

Initially, memory was thought to be unitary, until the idea of multiple memory system arose. Many different multimemory models have been proposed and supported. One makes the distinction between a declarative system, responsible for learning facts and events, and a nondeclarative system, which is referred to as procedural memory and is responsible for motor skills and procedures.[9] A complimentary memory model proposes that declarative memory (episodic, semantic) is further separated into 2 different interacting systems: a semantic memory system, encompassing recall of concepts and general knowledge not associated with contextual information, and an episodic memory system, linked with recall of specific events encoded in relationship to their temporal-spatial context.[10]

A review by Smith[6] found little evidence for the role of sleep in the enhancement of declarative memory performance. It appears that the function of sleep deprivation would vary with different types of memory. There is evidence that declarative memory subtypes may be differentially affected by the lack of sleep[11] or by awakenings from specific sleep stages.[12] The type and complexity of the task and the influence of sleep stages with different parts of the nighttime sleep cycle have been shown to be critical.[6] In addition to changes in the sleep stages, sleep parameters (eg, the number of rapid eye movement episodes and spindles) have been shown to be important in intensive learning situations.[13-15] For example, researchers report increases in spindle density following learning in a variety of tasks.[15]

Event-related potentials (ERPs) provide a good tool to investigate the underlying neural mechanisms of cognitive processes. Past studies have suggested that the earlier ERP components within a latency of 80 to 200 milliseconds (e.g., N1-P2 complex) are linked with states such as fatigue, arousal, and vigilance.[16] In support of these findings, more recently it has been shown that the influence of sleepiness generally results in lower amplitudes and/or longer latencies in these early components.[17] Only a few ERP studies during sleep have involved complex tasks, and those studies report evidence of information processing during sleep relating to memory and semantic processing.[18,19] It has been well established that, during wakefulness, the N400 component is enhanced in response to word pairs or words in sentences that are semantically anomalous relative to a given context, the amplitude of this effect relating to the degree of effort required to integrate a word in its semantic context.[20-22] ERPs have been recorded dur-

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ing various sorts of declarative memory tasks during wake, and results have consistently shown that differential ERP responses to old (studied) and new items may be useful for studying memory and retrieval processes.[23] The most reliable ERP index identified in memory has been referred to as the Old/New effect. It corresponds to the facts that the ERPs elicited by the first presentation of a new item are more negative than those elicited by the second repeated presentation of the same item (old item).[24] This modulation is typically observed whether the items to be recognized are pictures, faces, or verbal material.[25,26] This effect appears to have a specific role in memory, since it is not observed for incorrect judgments, i.e., misses and false alarms.[27] The ERP Old/New effect develops approximately 250 milliseconds after a stimulus and lasts for a duration of 800 milliseconds. It is composed of a series of components or effects distinct by their timing, scalp topography, task correlates, and instructions.[24,28-30] Each of these effects reflects the contribution of a particular cognitive process to recognition. The main contribution to the classic ERP Old/New effect is provided by the modulation of 2 posterior components. The first is a parietal distributed negative wave (N400) that has been attributed to integration of the stimulus with the already-present information in memory (semantic knowledge). A reduction in its amplitude for repeated (old) items is interpreted as easier access to the trace.[31,32] The second component involves a late positive component, also termed P600.[33] The P600 has been attributed to elaboration or mnemonic binding that leads to formation or retrieval of an episodic trace consisting of the item and its context. The modulation of this component is thought to reflect the reactivation of memory representation and to constitute the substrate of episodic information retrieval.[34] As characterized previously, the P600 modulation is larger for old stimuli[23,35] than for new stimuli.

The recent development of topographic ERP studies has made it possible to dissociate a number of frontal components of the classic Old/New effect.[28,36] The frontal Old/New effect begins approximately at 250 to 350 milliseconds after the stimulus. One interpretation is that it reflects strategic control and contextual integration of the stimulus.[37] These effects are manifested by a decrease in the amplitude of the frontal component on old faces, as compared with new ones. It has been suggested that this anterior effect reflects the contribution of the prefrontal cortex to episodic memory. Thus, by utilizing "Old/New" effect protocol, indexes related to both semantic and episodic processes could be used to investigate the contributions of sleep on the different subtypes of declarative memory.

The goals of the present study were 2-fold. First, this study will verify that the classic Old/New effect can be detected after a long delay. Second, the use of such a protocol will allow us to study the differential influence of declarative (episodic and semantic) subsystems, with a delay when it is filled with wakefulness or sleep. To our knowledge, no study to date has used a protocol in which ERPs are recorded before and after such an extended delay to characterize declarative memory processes.

METHODS

Participants

Participants were paid volunteers, recruited by personal contact or by public announcement. Medical history, sociodemographic information, and inclusion and exclusion criteria were collected for each subject. Exclusion criteria were a past or current history of psychiatric, neurologic, or other medical condition. Subjects were also excluded if any of their first-degree relatives had a history of primary sleep disorder or major psychiatric illness. Any subjects with uncorrected visual problems were excluded. None were using medications with a known effect on the central nervous system or sleep. The final group of participants consisted of 13 right-handed adults (7 women, 6 men) aged from 21 to 39 years with an education level of 18.3 ± 3.9 years.

Procedure

To study the effects on memory, we adopted an experimental protocol similar to that of Jenkins and Dallenbach[1] that compared the effects of a night's sleep and a daytime wake period on recognition memory. Although the amount of specific sleep stages and sleep variables are unavailable, our primary purpose was to evaluate the ERP protocol. In addition, this study design attempts to minimize the potential negative effects of the sleep-recording apparatus on the quality of the subject's sleep.

The ERP protocol is a variation of the classic study test used in ERP memory studies but into which a night of sleep or an equivalent period of daytime wake was inserted between the learning and recognition test (Figure 1). Subjects came twice to the laboratory, once for the study (learning) phase and the other for the test (recognition) phase. ERPs were recorded during the recognition phase only. All conditions were counterbalanced to control

PHASE A[a]				PHASE B[a]		
Evening Acquisition (5:00 PM - 7:00 PM)	SLEEP[b]	**Morning** Recall (7:00 AM – 9:00AM)	> 3–7 days	**Morning** Acquisition (7:00 AM – 9:00 AM)	WAKE[b]	**Evening** Recall (5:00 PM - 7:00 PM)

Figure 1—Protocol for the Experiment. [a]Phases A and B were counterbalanced. [b]Time of testing during each session was kept constant.

Table 1—Laboratory Sleep vs Home Sleep Information

	Home	Lab	t(12)
SOL, min			1.78[a]
1-10	6	3	
10-30	4	5	
30-45	3	4	
> 45	0	1	
SLEEP DURATION , h[b]			
Morning questionnaire(3 days prior to testing)		7.0 ± 1.2	
Sleep agenda (weekdays)	7.2 ± .82		-.79[a]
Sleep agenda (3 days prior to testing)	7.7 ± 1.2		-1.7[a]
AWAKENINGS,no.			-.60[a]
0	4	2	
1-2	7	8	
3-4	1	3	
5	1	0	

[a]p > .10, NS pairwise t test between sleep at home vs. in the laboratory.
[b]Data are presented as mean ± SD

the effects of practice, and participants were randomly assigned to either condition. To limit the possible confounding effects of cognitive variations throughout the day, time of testing was kept constant (Figure 1). The night of sleep was spent in the sleep laboratory. Information regarding the quality of the night of sleep in the laboratory was obtained in the morning on a questionnaire (Table 1 and 2). For the daytime condition, the subjects were able to carry on their routine daily activities and then return to the laboratory for the recognition phase. Upon return to the laboratory, subjects filled out a daytime questionnaire reporting their activities and vigilance levels immediately prior to testing (Table 3). To ensure that sleep was equal in both sessions, participants were asked to fill out questionnaires about sleep habits, sleep quality at home and in the laboratory, and the Stanford Sleepiness Scale (SSS) (see Table 3).

Sleep Agenda

This measure allowed participants to self-report their sleep experience on a daily basis throughout the experimental procedure. The scale was used as a control to verify that the quality of sleep in the laboratory was no different than that of a typical night's sleep in the home. For a 3-day period before all ERP recordings and throughout participation in the experiment, the number of hours per night of sleep was reported on the sleep agenda and then calculated for each subject. Space was provided for comments such as the quality of sleep, alcohol consumed, medications taken, or physical complaints for each day.

Morning Questionnaire

This measurement asks participants to self-define as having problems sleeping in the laboratory. It estimates (in minutes) the amount of time it takes to fall asleep (sleep onset) or return to sleep after nocturnal awakenings and the number of hours of sleep 3 days prior to ERP testing. The information provided allowed us to determine the amount of sleep prior to testing, along with the presence of difficulty initiating and the absence of maintaining sleep in the laboratory (Table 1 and 2).

Table 2— Nighttime Laboratory Sleep Information

	Number (%)
NIGHTTIME SLEEP QUALITY , as compared with usual	
Less	3 (23)
Similar	8 (61)
Better	2 (15)
DREAMT	7 (54)
SLEEP DEPTH	
Light	1 (8)
Moderate	1 (8)
Deep	11 (85)

Stanford Sleepiness Scale

The SSS[38] is a frequently used measure of daytime sleepiness that provides a measure of affective evaluation. This scale was included on the Daytime Questionnaire and consists of 7-point scaled items ranging from 1 (feeling active and vital; alert; wide awake) to 7 (lost struggle to remain awake); a higher number indicates increased sleepiness (i.e., lower levels of arousal) (see bottom Table 3). The participants select 1 option that best described how sleepy they felt prior to testing. It was administered just before the daytime ERP test recording. For analysis, the scale was collapsed to 1 to 4 points, in which a higher number indicated increased sleepiness (i.e., lower levels of arousal) (see bottom Table 3).

Memory Task: Study-Recognition Test

Subjects sat in a comfortable chair in a sound-attenuated room. Stimuli were presented on a gray background at the center of a screen 56 cm away from the subjects, subtending a visual angle of 5º with an interstimulus interval of 4 to 5 seconds. Each stimulus remained on the screen for 1000 milliseconds and was replaced by a mask with the word blink for 600 milliseconds. During the study (learning) phase, the subjects were asked to memorize each stimulus. During the recognition phase, participants were required to indicate for each stimulus as accurately and quickly as possible whether it has been previously presented ('old') or not ('new') by pressing arrow keys on the computer keyboard using the dominant hand.

Stimuli

The learning of unfamiliar faces was used because face processing makes use of semantic information (age, sex, expression, or resemblance with known persons)[39] whereas their unfamiliarity necessitates the formation of a new trace that fosters episodic processes.[40] These stimuli coincided with those used in other papers[41,42] that comprised front-view color photographs of persons' faces. Each face has been quoted as neutral, friendly, or unfriendly by a large group of persons in a prior study.[43] The 160 faces chosen as stimuli for this experiment were those with the higher neutral scores. Eighty of these 160 faces were used for the day test; the other 80 were used for the sleep test. Of each 80-face series, 40 were used for the learning phase and also corresponded to the 40 "old" (during the recognition phase). The other 40 faces served as the "new" stimuli during the recognition phase.

Table 3—Daytime Session Information

	Results	p Value[a]
AMOUNT OF SLEEP , h[a]		.670
Sleep session	7.8 ± 1.1	
Daytime wake session	7.7 ± 1.0	
STANFORD SLEEPINESS SCALE		
Very Alert	4	
Alert	6	
Foggy	1	
Very Sleepy	2	

[a]Paired t-test comparing amount of sleep, in hours, in the 3 days before sleep or wake session. Data are presented as mean ± SD.
Data are presented as number of subjects in the category and are collapsed from 1-4.

Recordings and Signal Extraction

The electrophysiologic signals were recorded by means of an amplifier (S.A. Instrument Inc, San Diego, CA). The electroencephalogram was recorded from midline scalp electrodes (Fz, Cz, Pz) placed according to the 10-20 International System.[44] All channels were referenced to linked earlobes. Vertical and horizontal eye movements were monitored via electrodes respectively placed below and on the outer canthus of the left and right eyes. During the recording, the impedance of all electrodes was maintained below 5 KΩ. The electroencephalogram was recorded continuously with a bandpass of 0.01 to 30 Hz, digitized on-line at a rate of 250 Hz and stored along with the codes identifying the experimental condition, the stimulus onset, and the subject's response for subsequent off-line averaging. Off-line averaging was performed (InStep Systems, Ottawa, Canada) after electrooculogram correction using statistical software algorithms[45] and after rejection for epochs with amplifier blocking exceeding 100 milliseconds. ERPs for correctly identified new items and correctly identified old items were then computed separately from 0- to 1000-millisecond poststimulus onset with a 200-millisecond prestimulus baseline. The ERPs were baseline corrected with respect to a 200-millisecond prestimulus recording interval for all sites, during both sessions.

ERP positive (P) and negative (N) peaks were identified by visual inspection of each participant's waveforms recorded at Cz within stimulus onset to 800 milliseconds. This epoch was selected as typical for previous studies of ERP Old/New effects. Peak amplitudes were quantified with respect to the baseline within time windows (see below) centered on the peak. As in our previous studies, the first component was a negative peak at 258 milliseconds after the stimulus. The N250 was analyzed in a 205- to 311-millisecond time window. The other components were a P350, (312-416 ms), a N400 (417-558 ms), and a P600 (559-753 ms). This procedure resulted in nonoverlapping time window of varying duration that allowed us to capture amplitude effects separately for each component.[46] Behavioral performance was obtained simultaneously with electroencephalographic data. Behavioral performance assessed on the scores (percentage correct and percentage missed) and reaction times (RTs). RTs were collected only for correct trials.

Statistical Analysis

Home and laboratory sleep data were compared with 2-tailed paired t-test. The effect of sleep and wake on cognition scores (percentage correct) was tested with a repeated-measure analysis of variance (ANOVA). RTs obtained were compared by means 2-session (sleep/wake) × 2-condition (old/new) ANOVA with repeated measures on subjects.

The ERPs were analyzed by a 2-session (sleep/wake) × 2-condition (Old/New) × 3-site (Fz, Cz, Pz) ANOVA with repeated measures. The Greenhouse-Geisser[47] nonsphericity correction was employed in repeated measures ANOVA when appropriate. Following convention, unadjusted degrees of freedom are reported along with the Greenhouse-Geisser adjusted p value. Main effects are reported first but described only if they did not interact with other variables. Statistical significance is assumed at α .05 level.

RESULTS

Experimental Measures

Morning Questionnaire

Table 1 shows the results of a paired t test between the laboratory and home sleep. It was concluded that there was no significant difference between the mean number of hours in the morning after sleeping in the laboratory versus those reported at home on the sleep agenda 3 days prior, $t_{12} = -1.7$, $p = .10$, NS or with those reported daily on the sleep agenda (weekdays), $t_{12} = -.79$, $p = .44$, NS) Furthermore, there were no significant changes in the time it took to fall asleep or mean number of nocturnal awakenings between the 2 scores (lab vs home) (see Table 1). Seventy-six percent of the subjects reported a similar to better quality of sleep in the laboratory, as compared with at home. In addition, the depth of sleep in the laboratory in 11 out of 13 (85%) of the subjects was reported as deep (see Table 2).

Daytime Questionnaire

Participants were asked to record the total sleep time at home 3 days prior to the daytime session test, and a paired-sample t-test was used to evaluate the data. The results showed no significant difference between the hours of sleep prior to daytime ERP testing and that in home ($t_{12} = 43$, $p = .670$, NS) (Table 3).

Behavioral Data

Performance following sleep was significantly better then following wake; as illustrated in Figure 2, there were significantly more correct responses ($F_{1,12} = 7.86$; $p < .02$) on the Old stimuli after a night of sleep. ANOVA on the scores for the previously studied stimuli (Old) revealed that there was a significant difference between nighttime sleep (mean ± SD) (76.3% ± 11.8%) and daytime wake (64.4% ± 12.7%) on accuracy performance.

The ANOVAs on correct-answer RT data showed a significant effect of condition (Old/New) ($F_{1,12} = 10.65$; $p = 0.007$). There was no significant effect of Session or interaction between the 2 factors, indicating that the subjects' Old/New effect on RTs was equally present both after the night or day session. The Old versus New items were recognized faster both after sleeping (mean ± SD) (1121.0 ± 296.1 ms vs 1183.9 ± 335.5 ms) and after a period of daytime wakefulness (1103.0 ± 404.2 ms vs1144.9 ± 425.7 ms).

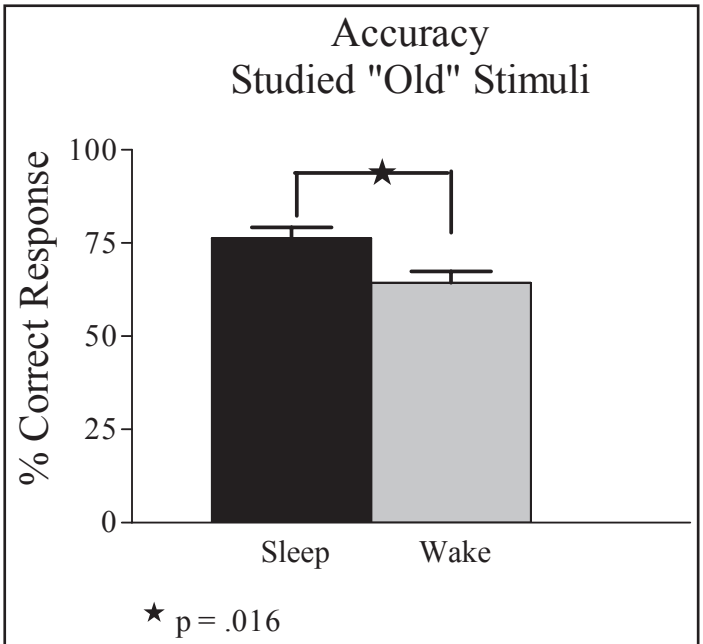

Figure 2—Behavioral performance (mean % and SEM) results showing that less correct responses for the old or previously studied stimuli were produced following a period of daytime wake vs. nighttime sleep.

ERP Data

The grand average waveforms presented in Figure 3 shows 4 main peaks associated with the Old/New effect, similar to those previously reported and for those reported in a similar design after the normal sleep and daytime wake conditions.[48] In both sessions, similar components were identified with slightly different window latencies.

Effects of Arousal, Fatigue, and Vigilance

N1-P2 Complex

The ANOVA for the N1 component showed a significant main effects of Site ($F_{1,12}$ = 10.63; p < .01) but no main effects or interactions involving the other 2 factors. Further analysis of the P2 component showed no significant main effects for any of the 3 factors or interactions.

Memory ERP Components

N250-P350 Time Window

The ANOVA for the N250 time window resulted in a significant main effect of Site ($F_{2,24}$ = 22.21; p < .001). There were also significant interactions between Session and Condition (Old/New) ($F_{1,12}$ = 14.66; p = .002) and a significant Site by Condition by Session 3-way interaction ($F_{1,12}$ = 4.28; p = .04). Further analysis on the N250 component showed that the Old/New effect was significant after the nighttime sleep session ($F_{1,12}$ = 11.86; p = .005) but not after the daytime wake session ($F_{1,2}$ = 4.00; p < .07).

Similarly, ANOVA on the P350 time window resulted in significant effect of Site ($F_{2,24}$ = 26.06; p < .001) and a significant interaction between Session and Condition (Old/New) ($F_{1,12}$ = 7.58; p < .02) but no other interactions. The P350 component showed a trend in the Old/New effect after both the sleep (v = 4.32; p = .06) and the daytime ($F_{1,12}$ = 3.44; p < .09) sessions. Figure 4 shows the generally larger effect after sleep at the frontal site and an interaction involving the daytime wake session.

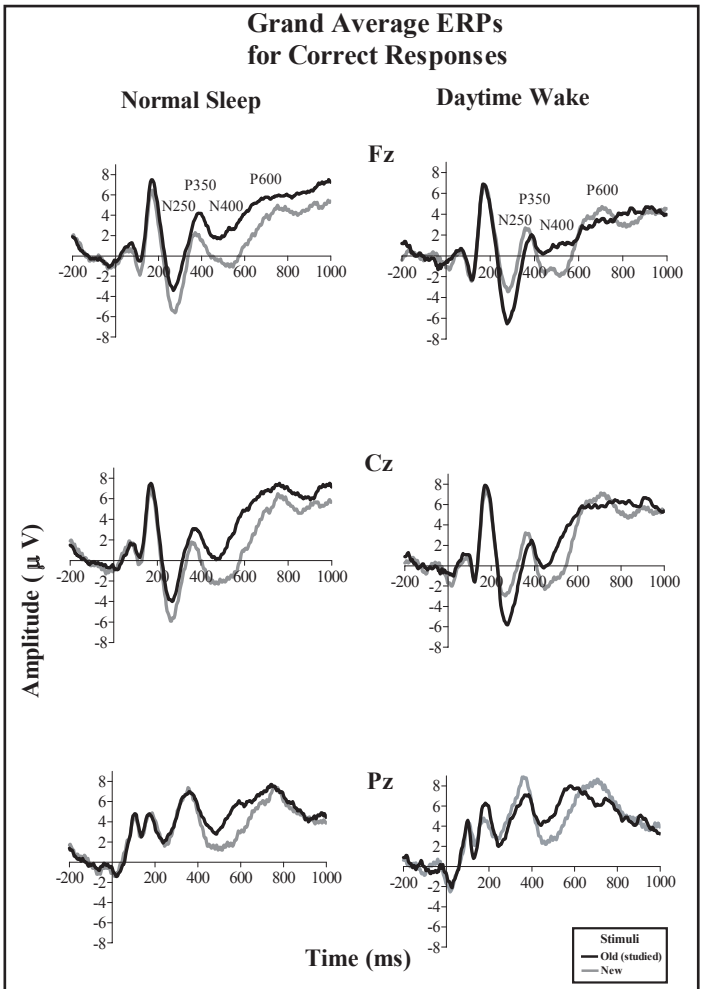

Figure 3—Grand average event-related potentials (ERPs) elicited by correctly recognized old or studied stimuli (black line) and new (grey line) at the midline (Fz Cz, Pz) sites. Left: Normal sleep session; Right: Daytime wake session. Four peaks appear at 250, 350, 400, and 600 ms after the stimulus, respectively.

These results indicate that ERPs within the N250 and P350 time window are differentially modulated by the Old/New effect in night and daytime wake sessions, and this effect is significant for the N250 ($F_{1,12}$ = 4.28; p = .04) and P350 ($F_{1,12}$ = 7.58; p < .02) complex at the frontal site after the sleep session (Figure 4).

N400 Time Window

The ANOVA on the data obtained in the N400 time window showed significant effects of Site ($F_{2,24}$ = 4.11; p = .04) and Condition (Old/New) ($F_{1,12}$ = 6.28; p < .03). There were no interactions involving the other factors, indicating that the classic Old/New effect was present following a long period of either daytime wakefulness or after a night of sleep. Figure 5 (left) shows that the N400 Old/New effect was larger over the more fronto-central sites (Fz-Cz). These results indicate a shift in topography of the Old/New effect for the N400 component.

P600 Time Window

The ANOVA on data obtained in the P600 time window showed no main effects of any of the 3 factors. There was, however, a significant interaction between Session and Condition, i.e., Old/New, ($F_{1,12}$ = 6.24; p < .03). Planned comparisons performed sep-

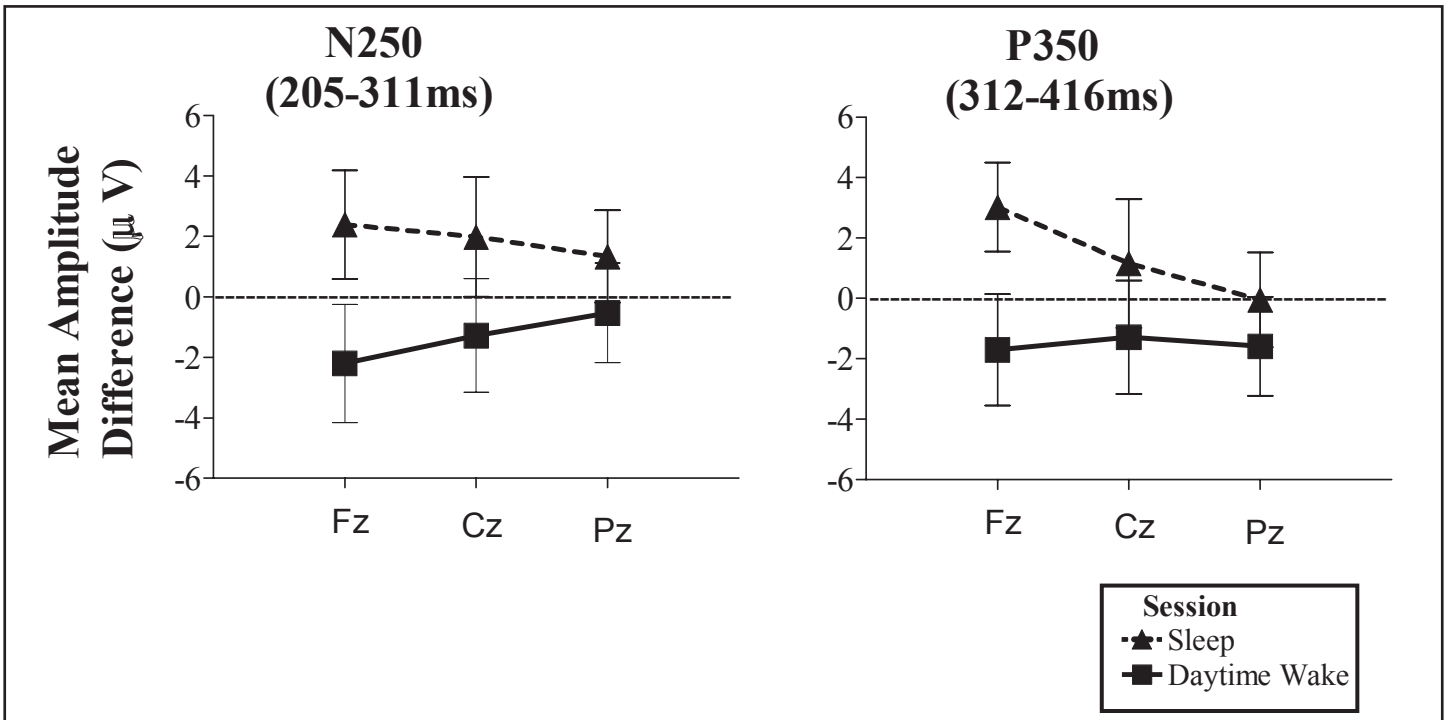

Figure 4—Mean amplitude difference (old minus new) for the N250 (left) and P350 (right) from midline (Fz, Cz, and Pz) electrodes corresponding to the early "Old" or "New" effect in the Sleep (dotted line) and Daytime Wake (solid line) sessions. Error bars represent the SEM of the old-new difference.

arately showed that the Old/New effect occurred following only the sleep session ($F_{1,12} = 13.73$; $p = .003$). Figure 5 (right) shows that the P600 Old/New effect is generally larger after the subjects slept.

The grand average (Figure 3) suggests a latency shift for the Old versus New stimuli following the daytime session. To test for this effect, an additional analysis was carried out on the P600 peak latency, defined as the maximum amplitude at Pz within 558 to 753 milliseconds. The analysis consisted of a 2 (Session) × 2 (Condition) design that showed no significant effect or interaction.

DISCUSSION

The first goal of the study was to examine whether sleep affects behavioral performance (eg, RTs, percentage correct) and the ERP Old/New effect differently than that seen after a period of wakefulness. The second aim was to establish if the ERP Old/New effect typically described after short time periods was also present after a long delay of a night of sleep or an equivalent period of daytime wakefulness.

Sleep Assessment

The results show that sleep prior to the ERP testing was no different than usual. Falling asleep and the number of nocturnal awakenings were also not different than those factors at home. Despite the fact that the night in the laboratory resulted in slightly less sleep than on the sleep agenda 3 days prior (39.6 minutes), the majority of the subjects reported sleeping deeply and having a moderate to high quality of sleep (Table 1).

Behavioral Data

As expected according to the literature,[24] participants' responded faster for the old studied stimuli compared to the new stimuli. However, there was no evidence for a beneficial effect of sleep on RTs. This indicates that the motor component of the Old/New effect does occur after a long delay, whether it is filled with sleep or wake.

On the other hand, participants made more accurate responses (percentage hits) after a night of sleep compared with after an equivalent period of daytime wakefulness. This enhanced performance could well reflect the role of sleep in memory consolidation. The idea is supported by the fact that the participants committed fewer miss responses (i.e., information actually forgotten) after sleep, which is consistent with the role of sleep in memory consolidation. Our results are in concordance with other behavioral sleep studies demonstrating a facilitatory effect on performance after sleep, compared with wake, on declarative memory tasks.[1,49,50] Along the same lines, Ficca et al[51] have shown reduced performance on morning recall in young adults when a night of disturbed sleep cycles occurred but not if the sleep-cycle organization remained preserved. This indicates the importance of the non-rapid eye movement/rapid eye movement cycle organization in recognition memory tasks. In our study, the number of nocturnal awakenings following the sleep session was similar to that in the home. This suggests that sleep-cycle organization was preserved and may have contributed to the improvements in accuracy performance.

Alternatively, the effect of sleep on memory processing may reflect circadian influences on the time of testing. Past research in this area has shown increases in performance in college-aged participants if tested at their "optimal time of day," i.e., in the afternoon, but not if tested at their "worse time of day," i.e., in the morning.[52,53] The pattern of our data, however, showed an opposite effect during the recognition test: after a night of sleep, there was more-accurate performance in the morning recognition test than after a period of daytime wakefulness. We also found no dif-

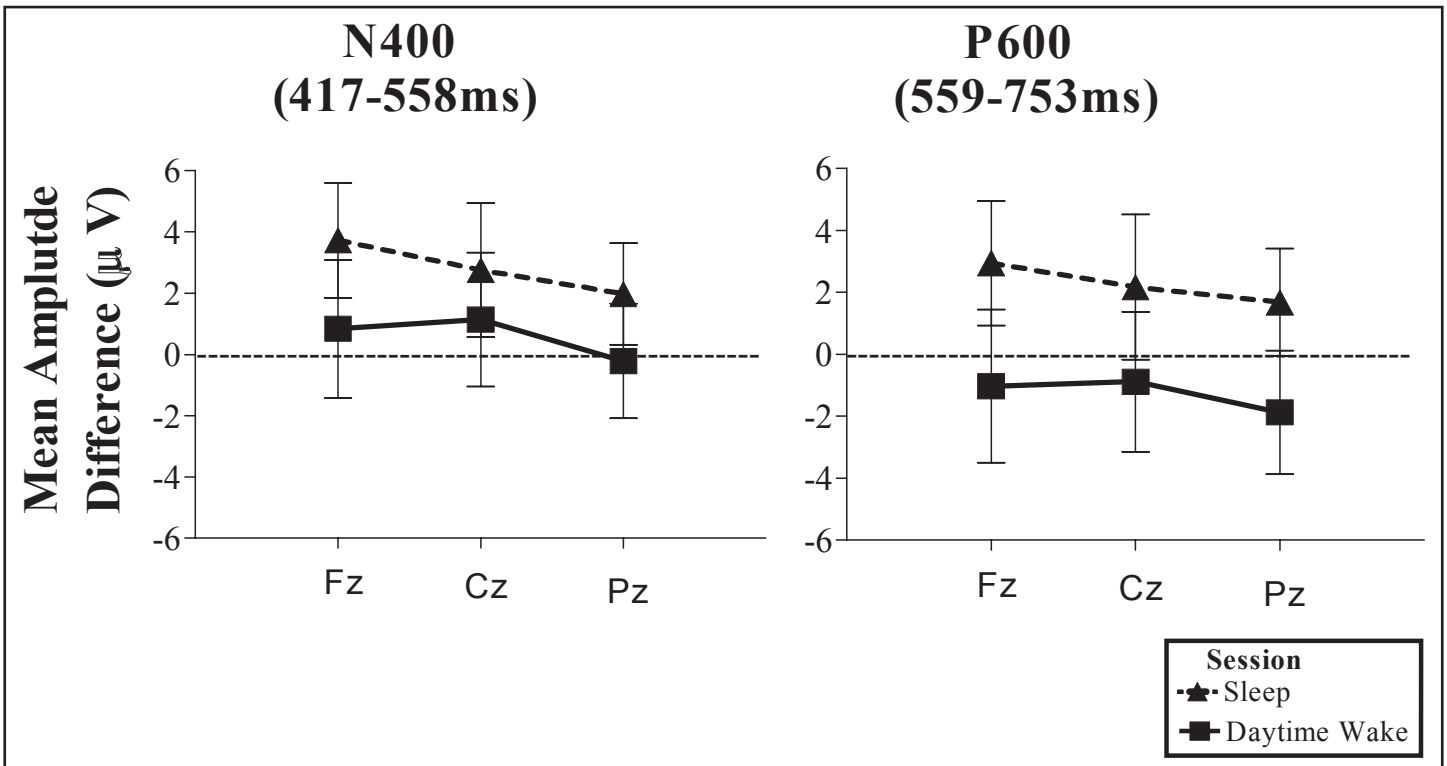

Figure 5—Mean amplitude difference (old minus new) for the N400 (left) and P600 (right) from Fz, Cz, and Pz electrodes corresponding to the late "Old" or "New" effect in the Sleep (dotted line) vs Daytime Wake (solid line) session. Error bars represent the SEM of the old-new difference

ference in RT measures for the recognition test at the evening and morning times, which would argue against circadian influences. It is possible that the impairments in accuracy performance during the wake session may be attributable to poor encoding of material that would lead to an increase in false alarms (i.e., an inability to discriminate new from old items) on the recognition test.[54] However, we did not find this to be the case, since our data revealed an increase in the number of miss responses (forgotten items) and very few false alarms.

ERP Data

Effects of Arousal (N1-P2)

As mentioned previously, the earlier ERP components identified in this study (i.e., N1-P2) have been linked to arousal[55] fatigue and vigilance[16] and have been reported to be diminished with drowsiness and in sleep. Therefore, the lack of a difference between sessions on N100 and P200 amplitudes indicates that any differences found on the later ERP components cannot be explained by differences in levels of arousal, fatigue, or vigilance across sessions.

Memory ERP Effects

In general, the results from the later components showed that the ERP to old stimuli differs from the ERP to new stimuli. That is, an Old/New effect is elicited after a long delay in the same way that numerous other researchers have shown this effect using shorter delays.[23-25,56-58] This finding further validates our protocol from an ERP perspective. Additionally, our results show differences in the Old/New effect across sessions. The magnitude of the effect is generally larger after sleeping, as compared with after a period of wakefulness, which is in agreement with a role of sleep in declarative memory consolidation. Moreover, it shows that sleep does not affect the later ERP component homogeneously. To the extent that the various components contributing to the Old/New effect are associated with distinct aspects of declarative memory (i.e., semantic and episodic processing) or with the activity of the frontal coordinating systems (see introduction), this observation indicates that sleep influences these processes in a differential manner.

Within the N250 to P350 time window, the results showed an early Old/New effect that is frontally distributed and is larger after sleep than after wakefulness. Recently, there have been a growing number of studies showing modulation of these components by contextual processing.[36,59,60] Similarly, our results indicated that sleep influences context processing differently than does wakefulness. In the same vein, there have been studies supporting the role of sleep in context processing. For instance, Harrison and Horne have shown that individuals deprived of sleep can correctly recognize previously presented stimuli (eg, faces) but have difficulty in remembering in which set of stimuli the faces had appeared (i.e., the source of information).[11] This difficulty in context processing has been further associated with the sensitivity of the frontal-cortex function to sleep loss,[61] which is consistent with the scalp topography reported here.

More precisely, studies investigating the frontal ERP components during memory tasks have shown more positive amplitudes in conditions that require the subject to retrieve contextual information (eg, the source) associated with the stimulus.[60,62,63] Another study using face stimuli showed that this effect is elicited automatically because it is present in both implicit/procedural and explicit/declarative tasks. In this regard, the more positive amplitude observed for old stimuli after sleep would indicate that greater effort is required to reintegrate the contextual details with the information following a night of sleep, compared with following a period of daytime wakefulness. How could this as-

sumption be consistent with the observed difficulties in context retrieval after sleep deprivation and with the consolidation hypothesis? Consolidation is a mechanism by which the trace of information in memory becomes "stronger" by being integrated in memory. Integration means that the information and the episodic contextual attributes with which it has been encoded are merged with previous semantic knowledge into a more abstract and distributed representation. Therefore, to be accurately retrieved on a subsequent presentation, a consolidated trace would necessarily have to be "re-contextualized." This may explain why, in our study, greater contextual processing effort is elicited after sleep, whereas after wake the reverse is observed (see Figure 3, Fz-Cz sites). Conversely, after a period of wakefulness, the information and its contextual attributes are likely to remain associated into an episodic representation, hence requiring less processing effort. On the other hand, sleep deprivation would impede consolidation (i.e., abstraction), with the consequence that the episodic links between the information and its context are lost and thus less likely to be retrieved. This may account for the results obtained in sleep-deprivation studies.

Our scalp-recorded ERP data were limited for further localizing this frontal effect. Expanding the ERP topography would allow further dissociation between 2 recently described frontal effects—a bilateral fronto-polar effect[28,41] and a fronto-central effect[37] that overlap with the N400 and P600 components—but differs in the functional meaning.[64]

The results from the subsequent time window showed an Old/New effect involving the posterior N400 component, similar to the effect classically observed after short delays. The consensual view is that the amplitude of this negative component is inversely proportional to the ease with which the information supplied by the stimulus can be integrated with the already-present information in semantic memory.[64-66] Accordingly, the decreased or more-positive amplitude to previously presented information (i.e., old stimuli) corresponds with the fact that it is more easily integrated than are the new stimuli. It follows that the lack of a difference between the daytime and nighttime sessions on the N400 Old/New effect would suggest that there is no facilitation by sleep on the integration process, which is a priori inconsistent with the consolidation hypothesis. However, recent studies using procedural tasks have demonstrated that consolidation is a 2-stage process.[67] The first stage, within 6 hours after learning, is a stabilization period by which the trace becomes more resistant to interference. This initial stage of consolidation occurs after learning during wakefulness. A potential ERP correlate of the initial stage of consolidation may perhaps be the N400-like component recorded by Brualla et al (1998) that persisted during sleep,[19] although there is no evidence to date that stabilization occurs during sleep. This may explain the lack of difference observed here on the N400 as well as on RTs (see above). The idea is further supported by the fact that the stabilization stage is accompanied by changes in the activity of the parietal and premotor cortexes,[68] consistent with the topography and neural generators of the N400.[41,69] The second stage of consolidation is the "enhancement" phase that occurs only during sleep and facilitates performance on subsequent trials. The higher scores obtained here after sleep versus wakefulness are consistent with this view. It is also supported by the effect of sleep on the earlier N250 to P350 frontal components that are consequent to the trace consolidation.

It could be argued that the facilitary effect of sleep on memory found in the present study does not reflect differences in memory per se but, rather, may be due to interference from subsequent information in the daytime. As previously mentioned, we found a significant difference in the N400 in the old (studied), compared with the new, stimuli, but there was no difference on the N400 component across session (Sleep/Wake). If one accepts that the N400 reflects the access to the memory trace, then the absence of a sleep-wake difference across sessions and no interactions involving the Session factor clearly indicate that the trace has not been erased by daytime interference. Further, if the N250 to P350 complex reflects contextual processing effort, then one would have expected larger amplitudes (i.e., greater effort) after wake to overcome interference after daytime wakefulness. However, our results show the opposite, that is, a larger N250-P350 effect after sleep. Interpreting our data in terms of the reconsolidation hypothesis or what we refer to as re-contextualization offers a more plausible explanation.

The N400 is typically followed by a late positive component or P600 that exemplify the Old/New modulation generally observed in memory studies.[66,70,71] However, our data show that the P600 Old/New effect occurred only after sleep. Characteristically, the functional interpretation of the P600 is that the amplitude of the P600 is proportional to the elaboration of the information retrieved from episodic memory.[18,72] By this account, the larger amplitude to old stimuli, as compared with the amplitude to new stimuli, simply reflects that previously memorized information accesses more-elaborated information than the new ones. Hence, our results indicate that information retrieved after sleep is more elaborated than after wakefulness, which is consistent with the enhancement phase of the 2-stage model of consolidation proposed by Walker et al. Similar to theN400, ERP studies showing that a P600-like component can be elicited during sleep[73,74] may well reflect that the processes underlying elaboration contribute to the sleepstage (i.e., enhancement) of consolidation.

An additional point concerning the P600 results in our study requires further comment, despite the fact that it was not found to be significant. After wake, there was a tendency of the P600 latency to old stimuli to occur earlier than for new stimuli, and it was also seen for the old stimuli after sleep (Figure 4). A longer latency of the late positive component has been related to increased task complexity[75,76] and higher workload. In the context of the present memory task, this can be best understood as the difficulty in making the recognition decision. By this account, the latency difference observed here in our study after wake would indicate that this decision is easier for old than for new stimuli, which is consistent with the stabilization stage of consolidation.

CONCLUSIONS

This study demonstrates that ERP (Old/New) effect on the declarative memory process is enhanced by sleep both in terms of behavioral performance and electrophysiologic measures. Furthermore, it appears that the various components and the changes in their parameters (i.e., increase vs decrease in amplitude and latency) permit inferences upon the influence of the different stages of consolidation on specific episodic and semantic processes involved in recognition. Although some of the observations remain to be confirmed, the protocol presented here could thus provide a useful basis to investigate further how sleep, wake, or sleep loss, affects declarative memory processes.

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