Sleep Spindles and Their Significance for Declarative Memory Consolidation

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Study Objectives: Functional significance of stage 2 sleep spindle activity for declarative memory consolidation.
Design: Randomized, within-subject, multicenter.
Setting: Weekly sleep laboratory visits, actigraphy, and sleep diary (4 weeks).
Participants: Twenty-four healthy subjects (12 men) aged between 20 and 30 years.
Interventions: Declarative memory task or nonlearning control task before sleep.
Measurement and Results: This study measured spindle activity during stage 2 sleep following a (declarative) word-pair association task as compared to a control task. Participants performed a cued recall in the evening after learning (160 word pairs) as well as in the subsequent morning after 8 hours of undisturbed sleep with full polysomnography. Overnight change in the number of recalled words, but not absolute memory performance, correlated significantly with increased spindle activity during the experimental night (r_{24} = .63, P < .01). Time spent in each sleep stage could not account for this relationship.
Conclusion: A growing body of evidence supports the active role of sleep for information reprocessing. Whereas past research focused mainly on the distinct rapid eye movement and slow-wave sleep, these results indicate that increased sleep stage 2 spindle activity is related to an increase in recall performance and, thus, may reflect memory consolidation.
Key Words: sleep, spindle, declarative, learning, memory, consolidation, reactivation, reprocessing
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INTRODUCTION

THE SUGGESTED FUNCTIONS OF SLEEP ARE MANIFOLD, INVOLVING ADAPTIVE STRATEGIES, PHYSICAL RECOVERY, ENERGY CONSERVATION, AND, RECENTLY, INFORMATION REPROCESSING. There is still no consensus regarding this issue, but a growing body of evidence is supporting the role of sleep for memory consolidation.[1-4] Recent studies indicate that slow-wave and spindle activity in non-rapid eye movement sleep (NREM), generated in the thalamocortical circuits, are involved in plastic neuronal modifications[2,5] and coordinated information transfer between different parts of the brain.[6]

For explicit memory, the integrity of a complex system involving the hippocampal formation and other regions of the medial temporal lobe is of major importance (for review see[7]). Animal studies have revealed that hippocampal neurons are involved in the "replay" of freshly encoded information. During posttraining (NREM) sleep, hippocampal neurons show similar firing patterns as compared to an encoding phase in which a particular type of task is learned.[8,9]

In animal research, a strong temporal correlation between the appearance of hippocampal high-frequency oscillations ("ripples") and spindles has been observed,[10,11] indicating a close association between the hippocampal memory system and mechanisms generating sleep spindles. The repeated activation of hippocampocortical and thalamocortical networks might provide the basis for the reorganization and consolidation of memory.

Recent studies with human subjects suggest a similar role of spindles for memory consolidation. With the exception of 1 study,[12] however, implicit memory[13-15] rather than declarative memory was investigated. Only 2 of these studies[12,15] focused directly on sleep spindles, demonstrating a learning- or experience-dependent increase in spindle density,[12] and/or stage 2 sleep duration.[15] The other studies[13,14] successfully related overnight improvement in performance to stage 2 sleep duration and, thus, indirectly to sleep-spindle density. Furthermore, there also is evidence that interindividual differences in spindle activity may reflect general differences in "learning ability," as demonstrated by a positive relationship between sleep-spindle density and full-scale IQ.[16] In the present study, we test the hypothesis that increased spindle activity in the experimental night following a declarative memory task is related to improved memory performance.

EXPERIMENTAL DESIGN AND METHODOLOGY

The present sample—consisting of 24 students (12 men) aged between 20 and 30 years (mean age = 24.4 years)—was part of a larger study, in which 2 subgroups were randomly assigned (parallel group design) to either (1) an implicit/procedural mirror tracing task or (2) an explicit word-pair association task. The study was conducted in the scheme of a joint research project between the Medical University of Vienna and the University of Salzburg using identical recording and testing material (NeuroScan Inc., El Paso, Texas). Participants in this study were right handed nonsmokers assigned to the explicit task.

Subjects were selected according to the following criteria: no history of severe organic and mental illness, no sleep disturbances [Pittsburgh Sleep Quality Index[17] Global Score (PSQI-TS

Disclosure Statement
This is not an industry supported study. Dr. Gruber is a part-time employee of The Siesta Group Schlafanalyse GmbH; and has participated in research projects on automated sleep analysis. Drs. Schabus, Parapatics, Sauter, Klösch, Anderer, Klimesch, Saletu, and Zeitlhofer have indicated no financial conflicts of interest.

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= 5] and no signs of mood disorders (Self-Rated Anxiety Scale[18] [SAS-raw score] < 36; Self-Rated Depression Scale[19] [SDS raw score] < 40). To control for sleep disturbances (sleep apnea, insomnia, periodic leg movements), all-night polysomnography (PSG) was performed prior to the experimental conditions. During the study period, all subjects had to report daily sleep habits and sleep quality by sleep logs, and their sleep-wake rhythm was monitored continuously by wrist-worn actigraphs. Subjects participated after giving written informed consent.

Subjects performed 5 different sessions in the (sleep) laboratory separated by 7 (± 1) days (cf. Figure 1, top). The entrance examination carried out 1 week before starting the investigation included documentation of the anamnesis and somatic findings, as well as various psychometric tests (among others PSQI, SAS, SDS).

The first night in the sleep lab served only for diagnostic and adaptation purposes. The second and third nights served either as control condition without intentional learning or as experimental condition with participants performing a declarative memory task (approximately 2.5 hours before sleep onset). The order of control and experimental nights were counterbalanced across subjects. After presentation of word pairs and pseudo-word pairs, recall and priming, respectively, were tested in the evening as well as on the subsequent morning (approximately 1 hour after the end of sleep). For the experimental condition, a third follow-up retrieval was conducted (in the morning) 1 week after learning. Before and after sleep, all subjects completed questionnaires for mood, drive, affectivity, and tiredness (100-mm visual analogue scales). All-night PSG started between 11:00 PM and 12:00 AM and was terminated after the subject's habitual total sleep time or after 8 hours of sleep.

For explicit declarative memory testing, an adapted version of the paired-associate word list task provided by Plihal and Born[20] was used. The adapted version aimed at reducing the close semantic relationship between the words of a pair in the original list. New pairs were created by randomly sampling words from the original list. The same set of 160 word pairs was presented twice in random order on a computer screen. Both blocks with 160 word pairs each were separated by a short break of approximately 2 minutes. Words were presented in "white" on a black background extending 0.8° in height. In the encoding session (preceding the experimental night), each word pair was presented for 1500 milliseconds, followed by a (white) centered fixation cross for 5000 milliseconds (during this time period subjects were instructed to encode semantic relationships between the words of a pair). Then the fixation cross-flipped from white to grey ("reference period," 3500 milliseconds). This was the signal for subjects to relax and await the next presentation. The encoding session lasted for 2 x 27 minutes. For a better control of mnemonic strategies, subjects were instructed to visually imagine a relation between 2 randomly related words (ie, from highly related word pairs like 'slippers – newspaper' or 'harp – painting' to unrelated pairs like 'attempt – steamer' or 'contribution – stone').

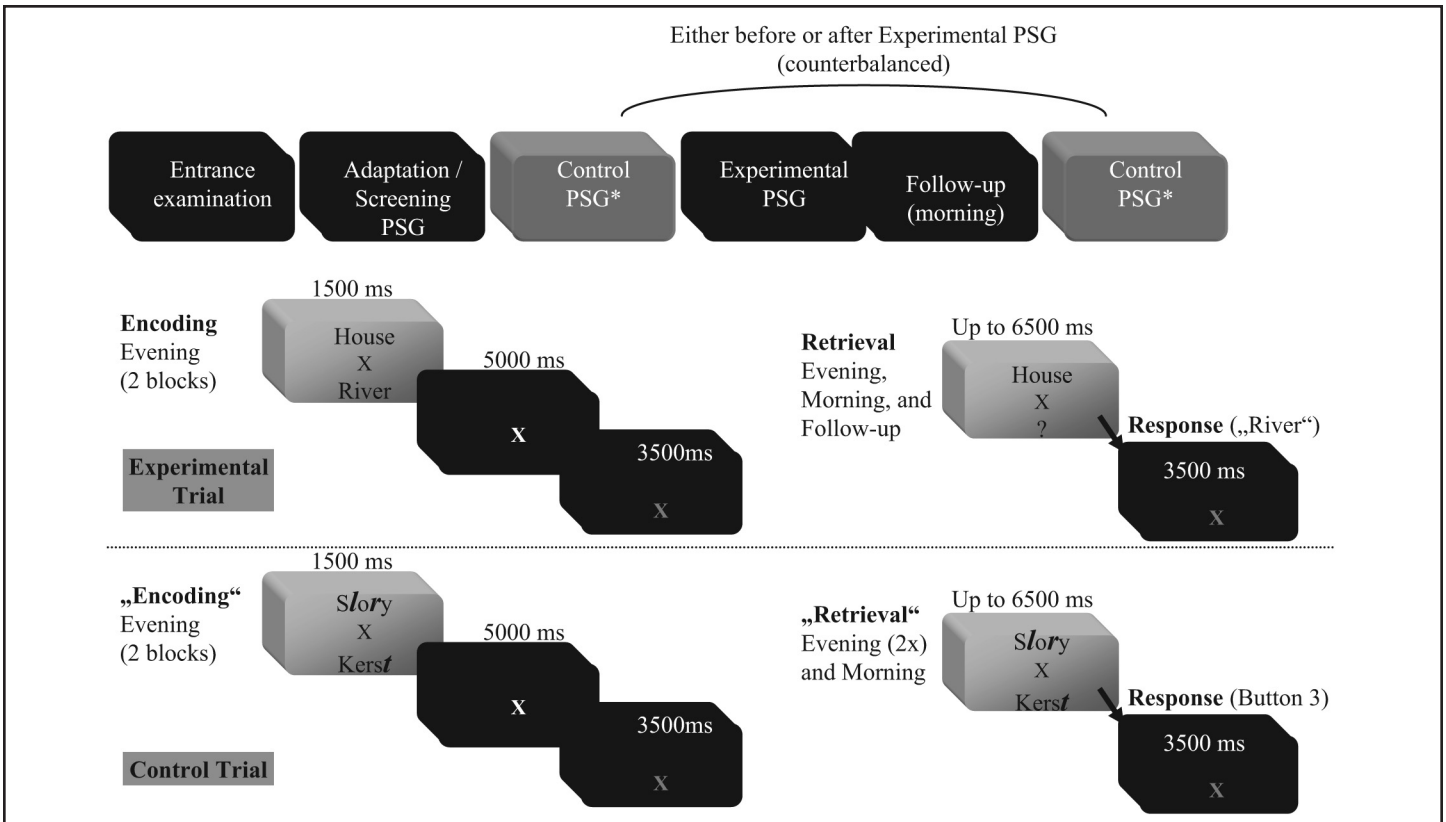

Figure 1—Study protocol and declarative memory task. In the top row, the weekly visits to the laboratory are depicted. The control night (grey) is scheduled either (*) before or after the experimental sessions. Follow-up retrieval (1-week after training) was only done for the experimental (memory) condition. The row below shows an experimental encoding trial (160 word pairs presented twice) before sleep as well as a retrieval trial, which was completed after training, in the morning after a night's sleep, and in the morning at follow-up. The bottom row shows a single trial for the control condition. Again each (pseudo-) word pair was presented twice, and subjects were instructed to silently count the number of deviant letters ("perceptual encoding"). Subsequently, subjects had to respond by pressing a button (1-4) to note how many letters they identified as deviant ("perceptual retrieval"). PSG refers to polysomnography.

After the encoding session, subjects performed a cued recall task with words presented in a different random sequence. Now, only the first word of a pair was presented, and subjects were asked first to press a button and then to report verbally the corresponding word (eg, 'river' in response to 'house') (see Figure 1, middle). The cued recall task was also performed in the morning after sleep and 1 week later (follow-up). At the end of the follow-up session, subjects were additionally asked to judge—for each word pair (on a 5-point Likert scale)—how easily the words could have been visually related during encoding.

The correct response score consisted of (1) the number of correct responses and (2) the number of (unambiguous) semantic correct answers (eg, 'flow' or 'stream' instead of 'river'), which was weighted by 0.5. The obtained values were expressed as percentages ([correct response score/160]*100) and are subsequently referred to as percentage "correctly retrieved."

The control task closely resembled the experimental task but did not include an intentional learning component. Instead of words, pseudo-word pairs were presented in which the appearance of some (lower case) letters was changed (Figure 1, bottom). Subjects were instructed to count silently all lower-case letters that were of both bigger size (1.1°) *and* written in italic font (a total of 1-4 in the 2 words) in the evening of the control night ("encoding") and subsequently had to indicate the number of these 'deviant' letters—of *both* pseudo words—by pressing 1 of 4 response buttons (control "retrieval"). In order to test *perceptual priming*—ie, a change in performance in response to a stimulus based on past exposure (eg, reflected in enhanced identification speed and accuracy)—subjects performed 2 blocks with identical pseudo-word pairs (160 each) but in different order during the evening. As in the experimental condition, the "retrieval" task also was performed in the morning after sleep, and likewise the change in (here, *perceptual*) performance from evening to morning was calculated. Note that due to technical problems, we are only able to report 23 reaction time (RT) values for the experimental task (1 missing) as well as 17 speed and accuracy values for the priming control task (7 missing).

The electroencephalogram (EEG) was recorded utilizing Synamps EEG amplifiers (NeuroScan Inc., El Paso, Texas). All signals were filtered (0.10-Hz high-pass filter; 70-Hz low-pass filter; 50-Hz notch filter) and digitized online with a 250-Hz sampling rate. 21 Gold-plated silver electrodes were attached according to the international 10/20 system (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, O2, as well as A1 and A2 for later re-referencing) and were referenced to Fcz. In addition, 5 electrooculogram (EOG) channels, 1 submental electromyogram (EMG) channel, 1 electrocardiogram channel (ECG), and 1 respiratory channel (chest wall movements) were recorded. During adaptation nights, *PSG recording* included 8 EEG, 4 EOG, 1 ECG, 3 EMG (submental and left/right tibialis), and 4 respiratory channels (nasal airflow, chest and abdominal wall movements, oxygen saturation). Sleep was scored visually according to standard criteria.[21]

Sleep spindles were detected automatically using the central electrodes (C3/C4), rereferenced to contralateral mastoids. Spindle detection was based on the following criteria: (1) 11.5- to 16-Hz band-pass filtering, (2) amplitude > 25μV, (3) duration > 0.5 seconds, and (4) controlling for muscle (30-40 Hz) and/or alpha (8-12 Hz) artifacts (see Figure 2; for details refer to [22]). Rather than measuring the mean number of sleep spindles per time (spindle density), the applied algorithm gives an integer value for the envelope spanning the respective wave complexes within a 30-second epoch (ie, capturing the duration as well as amplitude of identified spindles) and thus reflects the activity or intensity of the spindle process (termed SpA in the following). In order to derive a value rather "independent" of stage 2 sleep, we used the mean and not the sum of all of these values. Spindle activity (SpA) was analyzed during sleep stage 2 starting after 5 minutes of continuous sleep.

RESULTS

On average, subjects correctly retrieved 62.64% (SD = 20.6%) of all word pairs in the evening and 63.70% (SD = 20.4%) in the

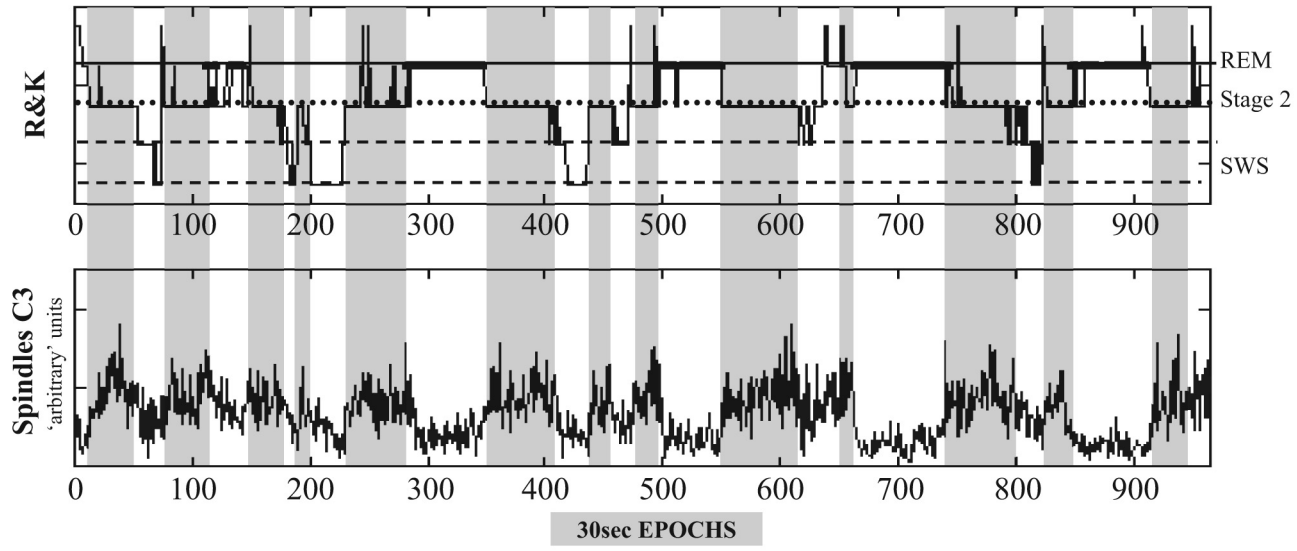

Figure 2—Spindle detection algorithm for a single subject. The top row shows Rechtschaffen and Kales (R&K) sleep staging for a single subject with rapid eye movement (REM) sleep (lined), stage 2 sleep (dotted), and slow-wave sleep (SWS) (dashed). The bottom row depicts the output of the spindle algorithm ('arbitrary' units) used for site C3. Note the increase in detected spindles during stage 2 sleep (shaded) and the marked decrease during REM and SWS.

morning after the experimental night. This score consisted of 59.86% (SD = 20.3%) hits and 5.70% (SD = 3.1%) semantically correct responses in the evening and 60.79% (SD = 20.4%) hits and 5.75% (SD = 2.7%) semantically correct responses in the morning. The score for correct retrieval dropped to 44.18% (SD = 17.7%) in the follow-up session a week later. Overall improvement between evening and morning recall, as measured by a paired-sample *t* test closely failed to reach significance (t_{23} = 2.03, P = .054). However, overnight improvement in reaction times (M = 2.56, SD = .56 and M = 2.25, SD = .55) was significant (t_{22} = 6.36, P < .001).

In the control task, subjects correctly responded in 91.14% (SD = 10.0%) to the number of deviant letters in pseudo-word pairs in the evening and to 92.13% (SD = 7.5%) in the morning thereafter. The improvement clearly failed to reach significance (t_{16} = .99, P = .34). Although, reaction times improved slightly overnight (M = 2.15, SD = .41 and M = 2.03, SD = .35), the effect was not significant (t_{16} = 1.92, P = .073).

Based on changes in spindle activity between the control and experimental night, 2 groups of subjects, 1 with enhanced spindle activity (termed 'SpA enhancers') and another without enhanced SpA activity ('SpA nonenhancers) were created by using 0 (no change) as a cut-off score (see Figure 3, right). A 2-way analysis of variance was calculated, with the within-subject factor BEFORE/AFTER (performance before and after the experimental night) and the between-subject factor SpA-ENHANCEMENT (SpA enhancers vs SpA nonenhancers). The dependent measure was memory performance. Results showed a significant main effect for BEFORE/AFTER ($F_{1,22}$ = 8.56, P <.01), but not for the between-subject factor ($F_{1,22}$ = 0.95). The significant interaction BEFORE/AFTER × SpA-ENHANCEMENT ($F_{1,22}$ = 10.61, P < .01) indicates that only for SpA Enhancers was retrieval in the morning significantly better than in the evening (cf. Figure 3, left). Note that the failure to see a main effect in *absolute* memory performance at both evening (t_{22} = - .79) and morning (t_{22} = - 1.16) between groups might simply reflect the lower power of between subject comparisons. Calculation of the same 2-way analysis of variance, but with perceptual performance (reaction time) as dependent measure (control condition), revealed no significant effects for BEFORE/AFTER ($F_{1,15}$ = 2.38), BEFORE/AFTER x SpA-ENHANCEMENT ($F_{1,15}$ = .97), and the between subject factor SpA-ENHANCEMENT ($F_{1,15}$ = .68).

Correlations (2-tailed) between spindle activity (control and experimental night) and *absolute* memory performance before (r_{24} = .28, P > .05; r_{24} = .24, P > .05) and after (r_{24} = .32, P > .05; r_{24} = .31, P > .05) sleep were not significant. However, correlations between spindle activity (experimental night) and changes in memory performance (after minus before) reached significance between evening and morning (r_{24} = .50, P < .05) but not between evening and follow-up retrieval (r_{24} = .03, P > .05). Changes in spindle activity (experimental minus control night) were an even better predictor for changes in memory performance between evening and morning (r_{24} = .63, P < .01; Figure 4) and between evening and follow-up (r_{24} = .47, P < .05). A partial correlation (2-tailed) controlling for the duration of sleep stages (1, 2, slow-wave sleep, and rapid eye movement) during the control and experimental night revealed an even stronger relationship between spindle activity and memory-performance changes for the former (r_{24} = .67, P < .01) but not for the follow-up session (r_{24} = .39, P > .05). For the control night, no significant relationship between reaction-time change and spindle-activity change could be observed (r_{17} = .43, P > .05).

In order to test the influences of stage 2 sleep duration, a 2-way analysis of variance with the within-subject factor CONDITION (control vs experimental night) and the between-subject factor

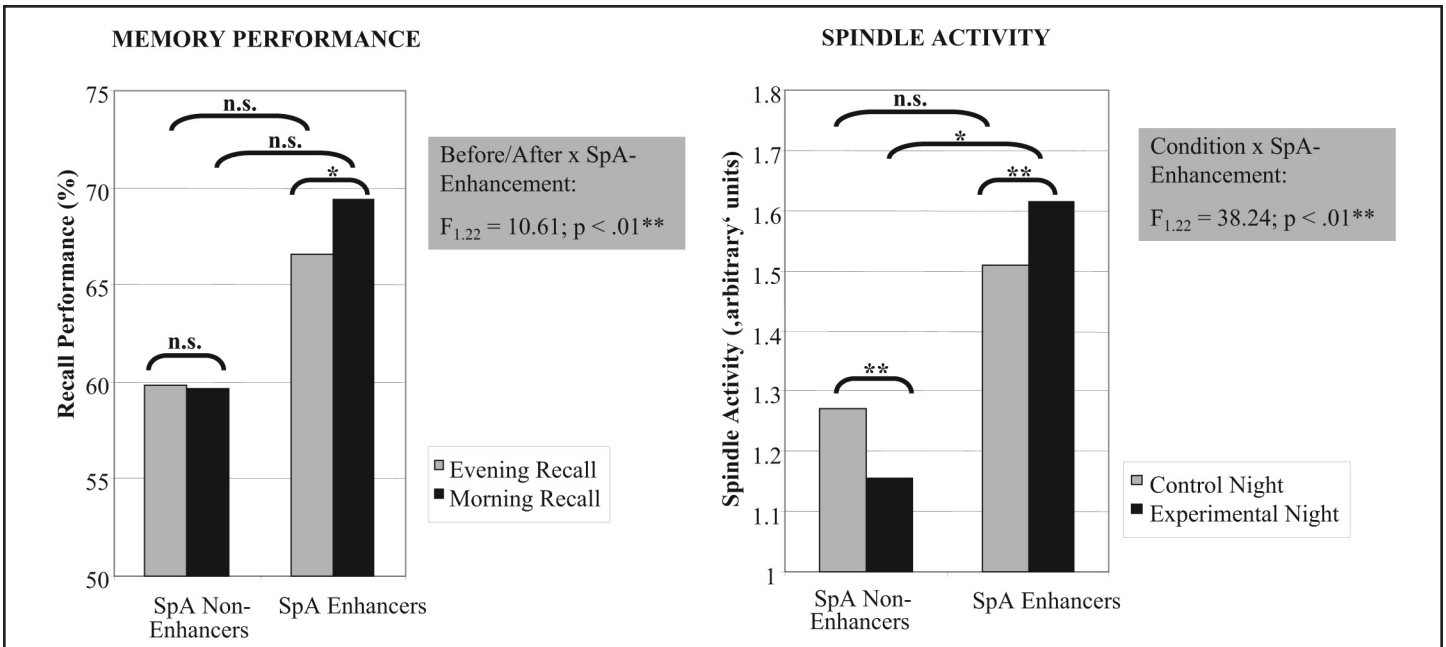

Figure 3—Two-way interactions depicting changes in word-pair recall (left) and spindle activity (SpA) (right) for SpA enhancers and SpA nonenhancers. Only those subjects having higher spindle densities in the experimental than in the control night ('SpA enhancers') show higher retrieval rates in the morning (after the experimental night) as compared to the preceding evening. Whereas SpA enhancers show a highly significant increase in SpA between control and experimental night, SpA nonenhancers show a highly signficant drop in SpA. Note that the 2 groups do not differ in the control night. Asterisks represent significance (*P*) of Bonferroni corrected 2-tailed *t* tests: * <.05; ** <.01; n.s., nonsignificant.

SpA-ENHANCEMENT (SpA enhancers vs SpA nonenhancers) was performed. The dependent variable was stage-2 duration. Results revealed no significant main effect for CONDITION ($F_{1,22}$ = 1.44) nor for the interaction CONDITION × SpA-ENHANCEMENT ($F_{1,22}$ = 3.49, P = .08) but a highly significant effect for the between-subject factor ($F_{1,21}$ = 11.42, P < .01), with SpA enhancers having more stage 2 sleep. The interaction CONDITION × SpA-ENHANCEMENT indicates a trend toward increased or respectively decreased stage 2 sleep duration (from control to experimental night) for SpA enhancers and nonenhancers. However, the correlation between changes in memory performance and change in stage-2 duration (experimental minus control night) was not significant (r_{24} = .20, P > .05). Additionally, the number of stage-2 epochs containing spindles (algorithm identified) was calculated in order to get a rough estimate of traditional 'spindle density.' Changes in the number of stage-2 epochs containing spindles (experimental minus control night), however, did not correlate with changes in memory performance (r_{24} = -.01, P > .05). Sleep parameters for SpA enhancers and SpA nonenhancers are depicted in Table 1.

To control for a possible influence of tiredness on overnight changes, another correlation was run between memory-performance change and tiredness changes (evening minus morning tiredness). However, the correlation proved to be nonsignificant (r_{24} = -.04, P > .05). A 2-way analysis of variance with the tiredness score as dependent measure and the within-subject factor TIME (before and after the experimental night) and the between-subject factor SpA-ENHANCEMENT (SpA enhancers vs SpA nonenhancers) indicates only a significant main effect for TIME ($F_{1,22}$ = 16.79; P = .003). The significant main effect TIME indicates that subjects were generally more tired in the evening than in the morning. Neither the interaction TIME × SpA-ENHANCEMENT ($F_{1,22}$ = 0.24) nor the between-subject effect ($F_{1,22}$ = 1.31) was significant.

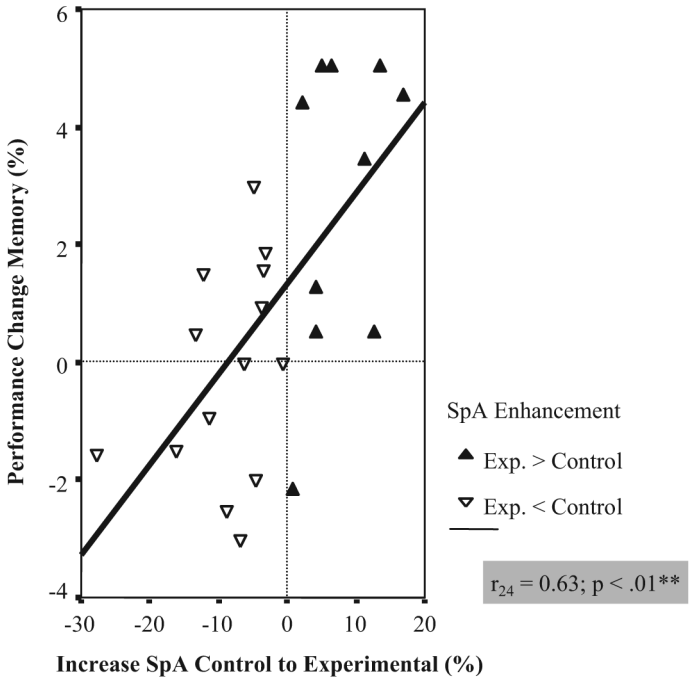

Figure 4—Relationship between spindle activity (SpA) and memory-performance change**.** Shown is a highly significant 2-tailed correlation (P < .01**) between SpA change (between the control and experimental night) and overnight change in recall performance. Note that preferentially 'SpA enhancers' (filled triangles) show the greatest improvement in performance.

DISCUSSION

Our findings provide evidence for the involvement of sleep-spindle activity in memory consolidation as measured by a declarative memory task performed before and after the experimental night. The fact that spindle activity is only related to changes in memory performance (increase or decrease over the night) but not to absolute performance is consistent with the hypothesis that spindle activity is specifically related to the consolidation of recently established memory traces but not to memory performance in general. It should be noted, however, that spindle activity in general (ie, experimental as well as control

Table 1—Time in bed, sleep efficiency, waking times, and time spent in each sleep stage for the control and experimental night in both spindle-activity enhancers and nonenhancers.

	Control						Experimental						Paired-samples *t* test			
	SpA Enh		SpA NonEnh		Student *t* test		SpA Enh		SpA NonEnh		Student *t* test		SpA Enh		SpA NonEnh	
	Mean	SD	Mean	SD	*t* value	*P* value	Mean	SD	Mean	SD	*t* value	*P* value	*t* value	*P* value	*t* value	*P* value
Time in bed, min	475.00	43.94	481.93	6.15	0.50	0.63	495.10	17.68	488.82	14.43	-0.96	0.35	-1.31	0.22	-1.58	0.14
Sleep efficiency, %	91.35	5.92	90.56	5.36	-0.34	0.73	85.96	12.76	89.00	7.45	0.74	0.47	2.03	0.07	0.78	0.45
SLAT, min	13.95	13.73	15.89	12.44	0.36	0.72	20.80	15.54	21.79	20.12	0.13	0.90	-1.54	0.16	-1.63	0.13
WTSP, min	24.55	21.18	27.89	24.54	0.35	0.73	45.40	54.66	27.96	31.94	-0.99	0.33	-1.74	0.12	-0.01	0.99
WAFA, min	1.85	5.85	0.11	0.40	-0.94	0.37	2.45	4.52	2.07	5.49	-0.18	0.86	-0.24	0.82	-1.38	0.19
Stage 1, min	36.35	14.55	41.21	15.59	0.77	0.45	40.35	13.81	41.21	16.73	0.13	0.89	-0.82	0.43	0.00	1.00
Stage 2, min	218.70	45.85	193.00	19.58	-1.67	0.12	217.05	41.51	178.39	29.02	-2.69	0.01	0.15	0.88	1.94	0.07
Stage 3 & 4, min	91.45	18.29	113.46	27.52	2.20	0.04	86.70	13.98	125.39	29.87	3.79	0.00	1.15	0.28	-1.63	0.13
REM, min	86.45	19.33	88.89	22.94	0.27	0.79	80.75	35.51	90.18	25.40	0.76	0.46	0.59	0.57	-0.21	0.84

Independent-samples *t* tests depict the differences between spindle-activity (SpA) enhancers and non-enhancers for both control and experimental night (light gray), and paired-samples *t* tests (dark gray) show the differences between nights in each group (both 2-tailed). Note the reciprocal relationship of stage 2 and slow-wave sleep between groups. All data are presented in minutes unless otherwise noted. SLAT refers to sleep latency; WTSP, wake within sleep period; WAFA, wake after final awakening; REM, rapid eye movement; Enh, enhancer; NonEnh, nonenhancer.

night) shows a trend toward a significant correlation (r_{24} = .31, P = .14 and r_{24} = .32, P = .13, respectively) with *absolute* memory performance in the morning (cf. Figure 3). In addition, this might point to a global relationship between sleep-spindle activity and "learning aptitude" (cf. Nader and Smith[16]).

The findings depicted in Figure 3 indicate that, as a group, only those subjects with an increase in spindle activity (SpA enhancers) from the control to the experimental night (cf. Figure 3, right) showed in average enhanced memory performance in the morning after the experimental night (cf. Figure 3, left). In other words, if a subject succeeds in elaborate encoding of newly acquired information, this will be reflected in an increase in spindle activity and subsequently increased memory performance. However, SpA enhancement does not interact with perceptual performance ($F_{1,15}$ = .97), and there is not a significant relationship between SpA change and change in perceptual performance (reaction times from evening to morning).

The results suggest that the increase in spindle activity cannot simply be accounted for by changes in (stage 2) sleep architecture, or subjects' tiredness. As revealed by partial correlations, the relationship between memory performance and spindle activity is not an indirect effect of sleep-stage durations. Even when all sleep stages are controlled, the correlation between memory-performance and spindle-activity changes remains significant (r_{24} = .67, P < .01). However, given the measure used for sleep-spindle activity in this study (*mean* across all stage-2 epochs), it requires clarification why SpA Enhancers still show an excess of stage 2 sleep ($F_{1,21}$ = 11.42, P < .01). At this point, we would simply suggest that participants showing a more intense spindle process are also more prone to (extensive) stage 2 sleep.

On the other hand, if the trend toward increased memory performance after a night's sleep (P = .054) would be solely an effect of circadian factors, a similar relationship would be expected for the perceptual control task. This however seems not to be the case, as perceptual improvement failed to reach significance for both the number of correct responses (t_{16} = .99, P = .34) as well as overall reaction times (t_{16} = 1.92, P = .073). Furthermore, note that there is neither an overall difference in tiredness between the 2 SpA groups ($F_{1,22}$ = 1.31), nor was there a significant interaction between tiredness (evening, morning) and SpA Enhancement ($F_{1,22}$ = 0.24).

Associations between sleep architecture and spatial memory,[15] motor-skill learning,[13,14] and implicit perceptual memory[23] are commonly reported, but evidence for improved performance in declarative tasks is rather rare.[20] It was also demonstrated[23] that the amount of time alone is inadequate to produce reliable improvement, while sleep or even short naps[24] improved performance on procedural tasks. However, we, as others,[12] did not find any absolute differences in memory performance between evening and morning word-pair recall, although the effect was nearly significant (P = .054). The reason for this might simply be due to fundamental differences to implicit memory tasks (eg, repetition learning, gradual skill retrieval) used in other studies. However, for the experimental task, reaction times were markedly accelerated after a night of sleep (t_{22} = 6.36, P < .001)

The relatively high retrieval rate of around 100 out of 160 words (63%) might be simply explained due to the chosen study sample (exclusively students) and the type of task. *Cued* recall tasks allow the use of powerful mnemonic strategies, like for example "imaging a visual relation." Furthermore, note that the learned word pairs are not collectively unrelated, but—as participants' ratings indicate—are well balanced between high (eg, market – potato) and low (eg, event – reserve) semantic relations.

Because of the prominent appearance of spindle activity at central electrode positions, we used central leads for spindle detection. However, it is known that slow (below 13 Hz) anterior and fast (above 13 Hz) more posteriorly located spindles can be distinguished,[25-27] suggesting the existence of at least 2—presumably functionally separated—spindle generators. It is still an open question whether these 2 sources contribute differentially to memory consolidation. Results from Gais et al[12] indicate that the largest learning-induced differences in spindle activity were observed at frontal leads, although spindle activity was generally highest at central electrodes. In contrast to Gais et al,[12] we did not generally find higher spindle densities after the experimental as compared to the (nonlearning) control night. Interestingly, however, we found a positive association between changes in spindle activity (control to experimental night) and memory performance (evening versus morning, cf. Figure 4).

In conclusion, the findings of the present study are in good agreement with the proposed role of sleep for information processing. In a similar way as was demonstrated in animal research, we may assume that the replay of learned information in hippocampocortical networks is temporally associated with the appearance of sleep spindle activity.[9,10]

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