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Interindividual sleep spindle differences and their relation to learning-related enhancements

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Abstract

We reported earlier that overnight change in explicit memory is positively related to the change in sleep spindle activity (between a control and a learning night). However, it remained unclear whether this effect was restricted to good memory performers and whether a general association of sleep spindles and a “sleep-related learning trait” may not account for this effect. Here we now present a secondary and more detailed analysis of our randomized multicenter study. Subjects were studied over a 4 week study period (including actigraphy and daily sleep diaries) including 3 overnight stays in the sleep laboratory. In the course of the study subjects completed test-batteries of memory (Wechsler-Memory-Scale-revised; WMS) and other cognitive abilities (Raven's Advanced-Progressive-Matrices; APM) and were asked to study 160 word-pairs in the evening before being tested by cued-recall. Afterwards subjects went to bed in the laboratory with full polysomnographic montages. Additionally, subjects participated on another occasion in a non-learning control (perceptual priming) task which was counterbalanced either before or after the learning condition. Slow as well as fast spindle activities were analyzed at frontopolar and central topographies. Although it was found that spindle activity is *generally* (in learning as well as control nights) elevated in highly gifted subjects, spindle analyses revealed that *spindle increase* (control to learning night) is specifically related to explicit memory improvement overnight independent of individual learning traits.

Together these findings suggest that the spindle *increase* after learning is related to elaborate encoding before sleep whereas an individual's general learning ability is well reflected in *interindividual* (and trait-like) *differences of absolute sleep spindle activity*.

Keywords

memory; spindles; EEG; trait; intelligence; G factor

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1. INTRODUCTION

Several lines of evidence support the hypothesis that memory traces and perhaps even insight and creativity benefit from sleep. More specifically, evidence accumulates which points to the importance of various sleep *mechanisms* for offline memory processing. Up to now, the “sleep and memory consolidation hypothesis” has received much empirical support from animal models (for review see (Peigneux et al., 2001) as well as from studies on implicit and explicit memory in human sleep (for reviews see Anderer et al., 2002; Maquet et al., 2003; Rauchs et al., 2005). The theory incorporates the concept of an offline replay or reprocessing of information (acquired awake) during sleep which has been previously shown in the animal model (Skaggs and McNaughton, 1996; Wilson and McNaughton, 1994). These studies revealed that during posttraining (NREM) sleep, hippocampal neurons show similar firing patterns (sharp wave/ripple activity) as compared to the encoding phase in which a particular type of information is learned. Additionally, temporal correlations between the appearance of hippocampal high-frequency “ripples” and sleep spindles have been observed by Siapas and Wilson (Siapas and Wilson, 1998) as well as Sirota et al. (2003). It has thus been speculated that spindles indicate the repeated activation of thalamocortical or hippocampocortical networks which are suggested as basis for reorganization and consolidation of memories (cf. Buzsaki, 1996; Steriade, 1999). An encouraging study by Rosanova and Ulrich (2005) recently demonstrated that indeed only neuronal firing patterns resembling those of sleep spindles are successful in inducing synaptic plasticity on a neocortical pyramidal cell level. Furthermore, there is nice evidence for hippocampal reactivations of previously learned episodic and spatial memories from the neuronal system level using functional neuroimaging studies of the human brain (Peigneux et al., 2004). Importantly, it could be shown in this study that these reactivation do indeed “matter”, as the hippocampal reactivations during NREM sleep were actually related to the behavioral improvement overnight.

In past sleep and memory research a main focus had been lying on “macroscopic” estimates of sleep, that is, the amount of REM or SWS (cf. Plihal and Born, 1997; Smith, 1995). Today however, specific sleep features and mechanisms are regarded as increasingly important for different types of offline memory (re-)processing. Especially, sleep mechanisms like sleep-spindles (Gais et al., 2002; Schabus et al., 2004; Smith and MacNeill, 1994), slow-waves (Huber et al., 2004), or the actual number of rapid eye movements (Smith et al., 2004) are being under active discussion. Besides memory consolidation constructs like “creativity” and “insight” seem to be animated by sleep processes (Wagner et al., 2004) and also an individuals “learning potential” is postulated to be reflected in certain sleep features like sleep spindles (Berner et al., 2006; Bódizs et al., 2005; Nader and Smith, 2003; Schabus et al., 2006) or REM density (Smith et al., 2004).

Earlier (Schabus et al., 2004) we reported spindle enhancement and memory improvement in a night after declarative word pair learning. However, memory improvers tended to have already more spindle activity in the control night and also slightly elevated starting performance before (post-learning) sleep. These circumstances raised the warranted question if not “both the spindle increase and the overnight improvement might reflect a more basic sleep-related learning trait.” (cf. Stickgold, 2004, p.1444). Therefore, we re-analyzed our data under special consideration of individual memory (Wechsler, 1987) and cognitive performance (Raven et al., 1998) measurements. The aim was to reveal whether only highly gifted subjects increase in spindle activity (from a control to a learning task) and memory performance overnight or whether spindle increase and positive memory change overnight is merely dependent upon elaborate memory encoding before sleep independent of general learning abilities.

Extending our previous work on sleep spindles (Schabus et al., 2004) we analyzed (i) frontopolar and central electrode sites and (ii) further examined the differential roles of *slow* and *fast* spindles in offline memory processing and its possible relationship with learning capabilities. The approach is driven by reports indicating 2 spindle types with slow spindles prevailing over anterior and fast spindles over centroparietal brain areas (Anderer et al., 2001; Werth et al., 1997; Zeitlhofer et al., 1997). Support for the differentiation of the two spindle types also comes from a recent simultaneous EEG and fMRI study which associated especially the fast spindle type with increased hemodynamic activity in hippocampal and sensorimotor regions (Schabus et al., 2007).

2. RESULTS

An overview over the behavioral data, sleep spindle estimates and sleep architecture divided for both APM-groups is provided in Table 1. As indicated by independent sample t-tests (grey shaded) APM groups only differ in (slow) spindle activity whereas sleep architecture and also memory improvement are not significantly different between groups. Paired-sample t-tests revealed no difference in sleep architecture (S2, SWS, REM [min]) between control and learning nights. Time spent in stage 2 sleep (min) is not related to spindle activity but positively related to the number of spindle detections (electrodes C3/C4: control night, $r_{24} = .68$, $P < .01$ for fast spindles; learning night, $r_{24} = .56$, $P < .01$ for slow and $r_{24} = .65$, $P < .01$ for fast spindles).

Spindle activity, explicit memory consolidation and its interaction with learning abilities

In order to test if spindle activity change (control to learning night) and/or memory improvement (pre- to post sleeping) is dependent upon memory or cognitive abilities we calculated 4-way ANOVAs $\text{CONDITION} \times \text{TYPE} \times \text{IMPROVEMENT}$ with the between subject factor WMS or APM, respectively. Analyses revealed no significant (corrected $P < 0.0125$) interactions with the between subject factors APM or WMS, however a trend at the frontopolar topography indicated that whereas both APM groups tended to have more fast spindles after learning than control, only APM+ performers also showed more slow spindle activity (after learning) ($F_{1,18} = 6.30$, $P = .02$; cf. suppl. Fig. 1, lower panel). Note that in the learning night slow (frontopolar) spindle activity is generally higher in highly gifted individuals (cf. Fig. 2, lower panels). Focusing on spindle activity change (and collapsing all slow and fast spindles) it was revealed that highly gifted memory improvers tended to have more frontopolar spindle activity as compared to moderately gifted memory improvers after learning ($t_{13} = -1.63$, $P = .13$, cf. suppl. Fig.2).

Furthermore, elevated spindle values were found for high cognitive performers (APM+) at the central topography ($F_{1,18} = 7.81$, $P = .01$) irrespective of condition, spindle type and memory improvement (cf. Fig. 3).

A general spindle type effect revealed, that as expected slow spindle activity prevailed at the frontopolar topography ($F_{1,18} = 17.37$, $P = .001$), whereas at central sites slow and fast spindle activity were equally distributed ($F_{1,18} = 0.14$, n.s.). Furthermore, it was found that exclusively memory improvers exhibit higher slow as well as fast spindle activity values in the learning as compared to the control night ($F_{1,18} = 8.61$, $P < .001$); non-Improvers on the other hand seemed to start at somewhat higher base levels and tendentially dropped in fast spindle activity after learning (central topography; cf. Fig. 4).

At the frontopolar topography a similar interaction nearly reached (Bonferroni corrected) significance ($F_{1,18} = 4.86$, $P = .041$; cf. supplemental Fig.1). The effect likewise indicated higher spindle values in the learning night for memory improvers only. Together this indicates, that although (i) generally elevated spindle values are found for high cognitive

performers (APM+) and (ii) fast spindle values are elevated after learning for memory improvers, no interaction is evident between this spindle enhancement, the memory change overnight and general learning traits (cf. Fig. 3). However, we cannot rule out the possibility that the post-learning increase in frontopolar (predominantly slow) spindling may also depend on general cognitive abilities (cf. suppl. Fig. 1-2).

Spindle features and explicit memory change

Please note that subsequently “relative” spindle measures (learning minus control -night values) are used which were correlated with overnight change in memory performance.

The increase in fast spindle activity at the central topography ($r_{24} = .48$, $P = .017$), as well as the increase in slow spindles at frontopolar sites ($r_{24} = .57$, $P = .003$) correlated positively with memory performance change. Breaking SpA into its components (amplitude and duration) it becomes evident that these enhancements can be largely attributed to an increase in fast spindle *amplitude* (C3/C4: $r_{24} = .52$, $P = .009$) and an increase in slow spindle *duration* (Fp1/Fp2: $r_{24} = .51$, $P = .012$) which are likewise correlated with memory change. Both the APM as well as the WMS test scores were unrelated to (control to learning night) changes in spindle activity or changes in the number of S2 spindles but related to (slow and fast) *absolute* spindle activities at the central topography (e.g., control, fast spindle: $r_{24} = .51$, $P = .011$). Results indicate that it is the respective *prevailing* spindle type (i.e., slow at frontal and fast at centroparietal sites) which is associated with the behavioral change overnight, but that the general level of memory or cognitive abilities is of less importance for these enhancements.

Correlating *absolute* slow and fast spindle activity to absolute memory performance before and after sleep revealed several significant effects at the central topography for the fast spindle type (control night: $r_{24} = .42$, $P = .044$ with pre-sleep performance; learning night: $r_{24} = .45$, $P = .028$ and $r_{24} = .45$, $P = .029$, for pre- and post- sleep performance, respectively). Note that these absolute relationships reflect a trait-like spindle effect, similar as the correlations with APM/WMS test scores do. Behavioral memory improvement is *not* significantly related to absolute spindle activities.

3. DISCUSSION

In the present study neither general memory abilities (as evaluated by the Wechsler Memory Scale-revised) nor general cognitive abilities (as evaluated by the Raven's Advanced Progressive Matrices) did have a major effect on the observed spindle enhancement (control to learning night) or overnight improvement (in explicit word-pair recall).

Note that the question arose because in a previous report - relating overnight memory improvement to spindle enhancement (i.e., higher SpA during the learning than control night) - the SpA enhancement group already showed trends towards higher memory performance before sleep (cf. Fig.3 in, Schabus et al., 2004). Commenting on that, Stickgold (2004) questioned if not “both the spindle increase and the overnight improvement might reflect a more basic sleep-related learning trait”. We thus examined whether only highly gifted subjects increased their spindle activity in response to (i) learning demands (i.e., in the post-learning night) and are (ii) as a consequence of their (more) *successful* memory encoding or more profound encoding depth (before sleep) also the only ones to benefit from sleep. Or more specifically -though speculative- are the ones to have more information to “replay” and thus exhibit sleep spindle increases and related behavioral improvements. However, we cannot rule out an alternative interpretation stating that more information encoded before sleep also means more information at risk to be lost which might oppose an advantageous effect of overnight improvement in highly gifted individuals.

Yet, present results indicate that spindle activity enhancements and memory enhancement – at least a central recording sites – can be seen irrespectively of “sleep-related learning traits” and are more related to whether subjects succeeded in elaborate encoding and overnight improvement in performance (cf. Fig. 3, right). That is, both good and moderate memory or cognitive performers (as assessed with WMS and APM, respectively) do show spindle enhancements if they are successful in encoding and offline information replay, and thus might show behavioral overnight improvements. Even more evident is the finding that highly gifted individuals do generally exhibit higher base levels of spindle activity (at central recording sites) in both control and learning nights (cf. Fig. 3; for details refer to Schabus et al. (2006). This robust relationship also becomes evident in significant correlations between absolute spindles measures and (i) APM/WMS scores or absolute (fast) spindles measures and (ii) memory performance before or after sleep which on their own can be understood as test of memory ability. Spindles recorded from the frontopolar electrodes revealed a more complex picture. Here we observed a trend for slow spindles only increasing (after learning) in the highly gifted individuals (cf. suppl. Fig.1-2, left). A definite answer on the relationship between learning-related night-to-night variations and interindividually strongly varying spindle base levels thus awaits further investigation.

In a study by Peigneux et al. (2003) post-training REM sleep reactivations were only observed in response to serial reaction time tasks with probabilistic but not random sequences which indicated to them that “...the processing of recent memories during post-training sleep does not seem to be initiated unless the material to be learned is structured” and meaningful to the subject. Extending this notion, we suggest that learning (before sleep) has to be *efficient* – or in other words has to have reached sufficient encoding depth - in order for offline processing during sleep to be initiated and becoming evident as enhanced sleep spindle activity in the sleep EEG. This idea that sleep-related alterations are dependent upon encoding depth before sleep is supported by a recent study from Schmidt et al. (2006) showing that sleep spindle changes are only observed after declarative learning in difficult (but not easy) associative encoding conditions. It has to be noted that in our data sleep spindle values did not merely increase (control to learning) as a result of learning before sleep, but rather that the effect is restricted to subjects who also behaviorally improve overnight (cf. Fig. 3-4; suppl. Fig.1-2). Probably, differences in the experimental design and spindle detection explain the discrepancy with the well known study by Gais et al. (2002) finding spindle density increase independent of overnight improvement in explicit word-pair recall. First of all, Gais et al. used exclusively unrelated word-pairs presented in pair lists (8 pairs each) allowing subjects to concentrate especially on difficult pairs during encoding. Secondly, traditional spindle density (i.e., mean number of spindles per 30sec) rather than spindle intensity was used as measure.

In our data at least the fast spindle increase control to learning night appears clearly related to subjects' overnight improvement (cf. Fig. 4) irrespectively of APM and WMS performance. We suggest that this subtle spindle activity change (to learning demands prior to sleep; Fig. 3-4, suppl. Fig.1) is crucial for subsequent memory consolidation. Although over a single night the behavioral effect might be quite small these subtle enhancements in spindling might be really advantageous for brain plasticity if expressed on a daily basis over years or even a life-time. Visually, one might conclude (cf. Fig 4, right) that non-improvers as compared to improvers show more fast spindle activity in the control night with this difference diminishing after learning. From this (however, statistically non- significant) observation one might speculate that only those subjects who have a remaining potential to generate more fast spindle activity in response to learning demands will also behaviorally benefit of post-learning sleep.

Interestingly, this spindle enhancement for memory improvers seems to be most strongly expressed in the respective topographical prevailing spindle type, that is in slow spindles at frontal sites (cf. suppl. Fig. 1, upper left) and in fast spindles at central recording sites (cf. Fig. 4, right). Although, literature strongly suggests the existence of two spindle types (Werth et al., 1997; Zeitlhofer et al., 1997; Anderer et al., 2001; Schabus et al., 2007) the present data does not indicate a clear involvement of either the slow or fast spindle type in the processing of declarative word-pairs. However, recent own data indicates that on a hemodynamic level slow spindles are generally associated with increased activity in the superior frontal gyrus, whereas fast spindles recruit a set of cortical areas involved in sensorimotor processing, as well as hippocampus (Schabus et al., 2007). Additionally, evidence is accumulating which assigns differential functional significance to the two types of spindles. It are mainly the studies by Clemens and colleagues which suggest task specific topographic distributions of sleep spindles. In accordance with known functional specialization Clemens et al. (2005) reported spindle foci over left frontocentral areas for verbal declarative memory but parietal spindle focus after spatial declarative learning (Clemens et al., 2006). Unfortunately, the authors did not distinguish slow and fast spindle types in their studies but given the literature (Anderer et al., 2001; Schabus et al., 2007; Werth et al., 1997; Zeitlhofer et al., 1997) slow frontal and fast parietal spindles, respectively, can be suspected. Interestingly, another group (Schmidt et al., 2006) likewise indicated lower frequency spindle increase over left frontal brain regions following another verbal declarative memory task. Last but not least, a recent study related power in the fast spindle range to procedural motor learning (Milner et al., 2006) well in agreement with fast spindle topography and its relation to sensorimotor activity during S2 sleep (Schabus et al., 2007). In order for in-depth analysis of sleep spindles and their site specific involvement in cognitive processing upcoming studies should begin to systematically investigate slow and fast spindles recorded from various scalp topographies.

In the present study specific sleep spindle features (i.e., amplitude, duration) were analyzed separately in order to identify the most important spindle characteristic being associated with their postulated information reprocessing function. Spindle feature analysis indicated that the stronger (amplitude) and longer (duration) - jointly combined in the measure “spindle activity” - spindles are during the learning as compared to the control night the higher the observed explicit memory performance change overnight. The single features spindle duration and amplitude, however, appeared to be less predictive of behavioral outcomes than their combination in the measure “spindle activity”.

Finally, it has to be mentioned that the behavioral improvements are indeed very subtle. Yet, in our view already a flattening of the otherwise strong forgetting curve (for *explicit* memories) is an indication for the beneficial role of sleep for memory consolidation. Therefore, we do not want to emphasize the memory “*improvement*”, but rather the *consolidation* of freshly encoded information and the *slowing down of the forgetting* process which seems to be associated with changes in human sleep spindle activity.

Certainly, the major draw back of the present study was the small sample size when separating subjects according to multiple criteria (i.e., general performance and overnight improvement; Fig. 2-3 and suppl. Fig.2). Further studies specifically addressing the interaction between sleep (spindles), general learning abilities, and overnight changes (in explicit as well as implicit memory tasks) are thus highly needed. Here we provided first results indicating that sleep spindle intensity increases only after *efficient* or *intense* declarative encoding before sleep. It is suggested that freshly encoded information is being processed during the night and thereby behavioral improvement becomes evident overnight. This increase in spindle activity is relatively small as compared to the large trait-like differences between subjects which are postulated to reflect important aspects of neuronal

(cortical-subcortical) network efficiency (Bódizs et al., 2005; Nader and Smith, 2003; Schabus et al., 2006). Importantly, we conclude that these two processes do coexist with the learning-related increase in spindles being widely independent of general cognitive and memory abilities.

4. EXPERIMENTAL PROCEDURE

Please note that this is a secondary and more detailed analysis of an earlier published study (Schabus et al., 2004).

Subjects

The study was performed in accordance with the Declaration of Helsinki, as revised by the World Medical Assembly at Tokyo and Venice and passed the local ethics committee. Subjects participated after giving written informed consent. Subjects of this study were twenty-four healthy volunteers (12 female, 12 male) aged between 20 and 30 years (mean age 24.42 ± 2.59) which were randomly assigned to an explicit word pair association task. Subjects were selected according to the following criteria: no history of severe organic and mental illness, no sleep disturbances (Pittsburgh Sleep Quality Index total score ≤ 5) and no signs of mood disorders (Self Rated Anxiety Scale raw score < 36 ; Self Rated Depression Scale score < 40). To control for sleep disturbances (e.g. sleep apnea, insomnia, periodic leg movements) a full all night polysomnography was performed prior to the experimental conditions. Participants in this study were students of medicine or psychology and were all right handed non-smokers.

Study design

Subjects performed five different sessions in the (sleep) laboratory separated by $7 (\pm 1)$ days (cf. Fig. 1). During the whole study period (4 weeks) subjects were monitored for regular sleep-wake habits by wrist worn actigraphs and asked to go to sleep between 11pm and midnight (as in the experimental nights). Likewise, sleep diaries were collected for the whole study period and it was reassured that subjects refrained from caffeine and alcohol prior to experimental visits. The entrance examination carried out one week before starting the investigation included documentation of the medical history and somatic findings, as well as various psychometric tests including the Advanced Progressive Matrices (Raven et al., 1998), and the Wechsler Memory Scale-revised (Wechsler, 1987). The first night in the sleep lab served for diagnostic and adaptation purposes. The second and third night served either as control condition without intentional learning (a perceptual priming task) 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 was counterbalanced across subjects. After performing the learning or control task subjects' performance was tested three times: immediately after learning (before going to bed), in the following morning (approximately one hour after getting up) as well as after 1-week (follow-up). All-night polygraphic sleep recordings (PSG) started between 11pm and midnight and were terminated after the subject's habitual total sleep time or after eight hours of sleep.

Experimental and control task

For testing declarative memory, a paired-associate word list task was used. The same set of 160 word pairs was presented twice in randomized order on a computer screen. In the encoding session (preceding the experimental night), each word-pair was presented for 1500 ms, followed by a centered fixation cross for 5000 ms during which subjects were instructed to imagine visually (encode) a relation between the words of a pair. Then the fixation cross flipped from white to grey which was the signal for subjects to relax and await the next

presentation. After the encoding session subjects performed a cued recall task with words presented in a different, randomized sequence. Now, only the first word of a pair was presented and subjects were asked first to press a button (for retrieval/reaction time) and then to report verbally the corresponding word (e.g., 'rive' in response to 'house'). The cued recall task was also performed in the morning after sleep. No feedback was given upon responding at recall testing.

The control task closely resembled the experimental task but did not include an intentional learning component (i.e., a perceptual priming task). Instead of words, pseudo-word pairs were presented in which the appearance of some letters was changed. Subjects were instructed to count silently all deviant (*italic* written) letters in the evening of the control night ("encoding") and subsequently had to indicate the quantity of these deviant letters (for details on task refer to Schabus et al., 2004).

Polygraphic recording

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 250 Hz sampling rate. 21 gold-plated silver electrodes were attached according to the international 10/20 system and were referenced to FCz. In addition 5 electrooculogram (EOG) channels, one submental electromyogram (EMG) channel, one electrocardiogram channel (ECG) and one respiratory channel (chest wall movements) were recorded. Sleep was scored visually according to standard criteria after re-referencing channels C3 and C4 to contra-lateral mastoids (A1 and A2, respectively). All-night sleep recordings were carefully checked for major artifacts and only electrodes of good signal quality throughout the night were included in further analyses.

Spindle analysis

Sleep spindles were detected automatically on anterior (Fp1, Fp2) and central (C3, C4) electrodes re-referenced to contra-lateral mastoids. Spindle detection was based on a new automatic algorithm (Anderer et al., 2005) which is a further development of the band pass filtering method developed by Schimicek et al. (1994). In a first step the EEG signal was filtered with a phase linear 4th order Butterworth band pass filter in the frequency range of 10-18 Hz and the envelope of the filtered signal was determined by Hilbert transformation. In a second step, sleep spindles were automatically identified based on the following criteria: (1) minimal amplitude of 12 μ V (2) spindle duration 0.3 – 2.0 sec and (3) a frequency range of 11-16 Hz. These thresholds were determined from the distribution of these variables in a polysomnographic pattern database including several thousand visually identified spindles from 189 healthy controls and 90 patients. Rather than measuring the mean number of sleep spindles per time (spindle density) the applied algorithm provides sleep spindle features such as the duration, amplitude and frequency and therefore reflects the activity or intensity of the spindle process. The used measure "spindle activity" (referred to as SpA) is composed of the mean amplitude and mean duration of stage 2 sleep spindle events (i.e., mean of [mean amplitude x duration of each single sleep spindle]; μ Vs). Additionally, time in stage 2 sleep and number of spindle detections are reported in Table 1 to also provide an estimate for traditional spindle density.

Event-related time-frequency analysis of spindles (using a Gabor filter) was done for 2.5 sec epochs (1000ms before to 1500ms after spindle onset) and for a frequency range of 1-30Hz over the (approx. 8 hour) night. Triggers for event-related spindle analysis were taken from both detected slow (=13Hz) as well as fast (>13 Hz) spindles and separately at each recording site.

Statistics

Cognitive and memory ability groups were created (based on percentile group) according to the subjects test scores on the APM and WMS-R (general), respectively. More specifically, subjects were grouped into 2 APM-levels (i.e., highly gifted or APM+ and moderately gifted or APM- subjects) and additionally into 2 WMS-R levels (good memory performers or WMS+ and moderate memory performers or WMS-) by median split. Additionally, subjects were assigned to two IMPROVEMENT groups according to their explicit memory change overnight. Subjects improving behaviorally overnight (termed “Improvers” in the following, $n = 15$) in the explicit memory task had memory enhancements between 0.5% and 5% and those failing to improve ($n = 9$) did have performance changes between -3% and 0.5%. This brings up 4 APM- “Non-Improvers”, 7 APM- “Improvers”, 5 APM+ “Non-Improvers”, and 8 APM+ “Improvers” included in the study sample.

4-way ANOVAs CONDITION (control, learning night) $\times$ TYPE (slow, fast spindles) $\times$ IMPROVEMENT (“improvers”, “non-improvers”) $\times$ APM and CONDITION $\times$ TYPE $\times$ IMPROVEMENT $\times$ WMS were calculated for two topographies (bilateral frontoparietal [Fp1, Fp2] and central [C3, C4] recording sites) to test for possible interactions between spindle activity, memory improvement (explicit word-pair association) and learning abilities. The dependent variable was spindle activity which implicitly reflects the duration and amplitude of the spindle process. In order to account for possible confounding influences of time spent in stage 2 sleep, stage 2 minutes were used as covariates in the repeated measures ANOVAs. Analyses of night halves with respect to their importance for memory improvement and general learning ability did not reveal a definite picture and were thus dropped for sake of simplicity. Multiple comparisons (2 topographies $\times$ 2 between subject factors) were met by using Bonferroni corrected p-values ($P < 0.0125$).

Furthermore, spindle activity was broken down into its initial components comprising spindle duration and spindle amplitude and correlations (2-tailed) were calculated for *changes* in these spindle features (and the overall number of detected S2 spindles) with memory improvement (evening to morning change in recalled word-pairs). Absolute spindle activity was additionally correlated to absolute memory performance pre- and post- sleep. Additionally, APM and WMS test scores were correlated with (i) absolute spindle activity, (ii) the changes in spindle activity and (iii) the change in the number of detected S2 spindles (between learning and control night). All measures distinguished between the slow (=13 Hz) and the fast (> 13 Hz) spindle type.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Study design. Illustrated are the subjects' five visits (3 PSG nights) to the sleep laboratory separated by one week each. During the whole study period (4 weeks) subjects ($N = 24$) had to wear wrist actigraphs to monitor their regular sleep-wake cycles and to complete daily sleep diaries. The order of learning and control tasks prior to sleep were counterbalanced across subjects (double-sided arrow) with the (1-week) "follow-up retrieval" session only following the learning task. PSG, polysomnography.

Figure 2.

Sleep spindle activity and its relation to memory improvement and cognitive abilities. Upper graphs depict moderately gifted subjects (APM-) and lower graphs highly gifted (APM+) subjects whereas on the left “Non-Improvers” and on the right “Improvers” are shown. Note that highly gifted individuals (APM+) have more activity in the slow spindle frequency band (11-13Hz; marked area) time-locked to the detected spindle onset ($t=0$) irrespective of memory improvement group. Colors represent the (mean) “power” (Gabor estimates; arbitrary units) of EEG frequency bands (between 1-30 Hz) with hot (red) colors indicating stronger activity. For the time-frequency graphs all-night (slow and fast) detected sleep spindles from frontopolar recording site Fp1 of the learning were used as “events” of interest.

Figure 3.

Spindle activity increase control to learning night is independent of APM performance. Control to learning night enhancement in spindle activity (central topography) seems only to depend on whether subjects are also memory improvers (right) or non-improvers (left) but not whether they are highly (solid) or moderately gifted (dashed line) as tested with the APM test. Furthermore, the overall higher base levels in spindle activity in high cognitive performers (APM+) irrespective of learning condition are evident. Post hoc statistics are indicated where significant. Note that control to learning night enhancements in memory improvers are independent of APM performance; the provided p-value (dark gray) refers to the general increase with both improvement groups collapsed.

Figure 4.

Slow and fast spindle activity during control and learning night for memory “Improvers” and “Non-Improvers” (central topography). Note that (i) the (fast) spindle increase control to learning night is dependent upon whether subjects are also memory improvers (solid line) and (ii) that although, memory non-Improvers seem to start of at higher spindle activity levels none of the between subject comparisons turned out to be significant. Mean spindle activity values ($\pm$ SEM) are depicted. Post hoc statistics are indicated where significant.

Table 1
Performance values and spindle measures (central topography, C3/C4) for highly (APM+; n=13) and moderately gifted (APM-; n=11) subjects.

As depicted highly gifted individuals had elevated (slow) spindle activity in both control and learning nights. However, the control to learning increase in spindle activity does not differ significantly between the two groups. Likewise, overnight change in memory performance is not different between moderately and highly gifted individuals. Absolute values of slow (=13 Hz) and fast (>13 Hz) spindle activity are provided. TIB, time in bed; SWS, slow-wave sleep (S3+S4); REM, rapid eye movement.

Explicit word-pair association					
	APM- performers		APM+ performers		t (P)
	Mean	S.E.	Mean	S.E.	
Performance (pre-sleep) %	56.46	7.40	67.87	4.35	-1.38 (.18)
Performance (post-sleep) %	57.00	7.23	69.36	4.29	-1.52 (.14)
Performance (follow-up) %	38.06	5.38	49.36	4.58	-1.61 (.12)
Memory improvement (in %)	0.54	0.66	1.49	0.78	-0.90 (.38)
Advanced Progressive Matrices (APM)	103.55	1.61	126.08	1.96	-8.67 (<.01)*
Wechsler Memory Scale (WMS-R general)	113.00	4.67	120.00	3.33	-1.25 (.22)
Control: slow spindle activity	14.15	0.44	16.73	0.64	-3.19 (<.01)*
Control: fast spindle activity	15.59	0.58	17.86	0.96	-2.03 (.06)
Learning: slow spindle activity	14.43	0.49	17.01	0.62	-3.17 (<.01)*
Learning: fast spindle activity	15.94	0.53	17.86	0.92	-1.81 (.09)
Control: slow detected spindles	364.36	73.68	625.46	92.18	-2.16 (.04)*
Control: fast detected spindles	1350.91	141.83	1289.31	122.27	0.33 (.74)
Learning: slow detected spindles	348.82	90.50	592.69	96.27	-1.82 (.08)
Learning: fast detected spindles	1241.27	153.42	1212.54	161.87	0.13 (.90)
Control: Total sleep time	436.23	8.18	434.08	10.62	0.16 (.88)
Control: S2 (Minutes, TIB)	207.95	8.80	200.12	11.00	0.54 (.59)
Control: SWS (Minutes, TIB)	96.14	7.58	111.19	7.17	-1.44 (.16)
Control: REM (Minutes, TIB)	90.09	7.83	86.00	4.67	0.47 (.65)
Learning: Total sleep time	435.41	10.06	427.04	16.34	0.42 (.68)
Learning: S2 (Minutes, TIB)	195.05	11.28	194.04	11.65	0.06 (.95)

Explicit word-pair association					t (P)
APM- performers		APM+ performers			
	Mean	S.E.	Mean	S.E.	
Learning: SWS (Minutes, TIB)	106.18	7.37	111.88	10.10	-0.44 (.66)
Learning: REM (Minutes, TIB)	87.77	6.65	84.96	9.91	0.23 (.82)