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Consolidation of temporal order in episodic memories

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ABSTRACT

Even though it is known that sleep benefits declarative memory consolidation, the role of sleep in the storage of temporal sequences has rarely been examined. Thus we explored the influence of sleep on temporal order in an episodic memory task followed by sleep or sleep deprivation. Thirty-four healthy subjects (17 men) aged between 19 and 28 years participated in the randomized, counterbalanced, between-subject design. Parameters of interests were NREM/REM cycles, spindle activity and spindle-related EEG power spectra. Participants of both groups (sleep group/sleep deprivation group) performed retrieval in the evening, morning and three days after the learning night. Results revealed that performance in temporal order memory significantly deteriorated over three days only in sleep deprived participants. Furthermore our data showed a positive relationship between the ratios of the (i) first NREM/REM cycle with more REM being associated with delayed temporal order recall. Most interestingly, data additionally indicated that (ii) memory enhancers in the sleep group show more fast spindle related alpha power at frontal electrode sites possibly indicating access to a yet to be consolidated memory trace. We suggest that distinct sleep mechanisms subserve different aspects of episodic memory and are jointly involved in sleep-dependent memory consolidation.

1. Introduction

The different functions of sleep have not yet been completely understood although some kind of involvement in memory consolidation seems to be widely accepted (for review see Diekelmann and Born, 2010). More specifically, sleep has been proven to enhance hippocampus dependent temporal sequence memory in

strengthens the original temporal sequence structure of a memory trace (Drosopoulos et al., 2007). In that study subjects were asked to learn triplets of words presented one after the other. Later, recall was tested by presenting word by word and asking which one came after the other. Sleep was found to enhance word recall, but only when students were asked to reproduce the learned words in the original forward direction (cueing with A and B and asking for B and C, respectively). Still debated, however, are the exact mechanisms which underlie the transformation of newly learned information into more stable forms during sleep.

Different sleep stages are assumed to be crucial for different types of memory. One of the main hypotheses, the "dual process theory", assumes that a specific sleep stage is characteristic for a specific memory type. Slow wave sleep (SWS) supports declarative memory consolidation whereas rapid eye movement (REM) sleep does so for procedural memories (Gais and Born, 2004; Maquet, 2001; Plihal and Born, 1997, 1999). The "sequential hypothesis" on the other hand, proposes that the alternation of sleep stages in cycles supports effective memory re-processing (Ficca and Salzarulo, 2004; Giuditta et al., 1995). This idea of complementary

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an essential role of SWS for system consolidation which is complemented by synaptic consolidation taking place during REM sleep. However, data directly supporting this latter hypothesis is still incomplete.

Neuronal replay during both SWS (Nadasdy et al., 1999; Wilson and McNaughton, 1994) and REM sleep (Poe et al., 2000), as usually observed in animal studies, seems to underlie the beneficial effect of sleep over wakefulness with regard to memory consolidation. Specifically, hippocampal replay during the night but also during quiet restfulness following spatial learning is a well-documented phenomenon (Frank et al., 2011; Zugaro and Girardeau, 2011).

Concerning memory relevant sleep features during the night, most empirical evidence is present for individual slow waves (Mölle et al., 2002), sharp wave ripples (Buzsaki, 1984; Mölle et al., 2009) and sleep spindles (Clemens et al., 2005; Fogel and Smith, 2006; Schabus et al., 2004). Here, the fast spindle type (>13 Hz) appears to be more relevant for sleep-dependent memory

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consolidation, specifically for motor memory formation (Morin et al., 2008; Tamaki et al., 2009). Additionally sleep spindles have been found to be significantly related to general cognitive abilities or "intelligence" (Bodizs et al., 2005; Fogel et al., 2007; Schabus et al., 2006).

In contrast to the idea of memory consolidation in sleep, EEG specific alpha oscillations seem to play an important role for successful memory reactivation during waking (Klimesch et al., 2006). In light of this data and the finding that sleep spindles are temporally linked to hippocampal reactivation (Siapas and Wilson, 1998) the question arises if alpha might not also play a crucial role during nightly "replay" or spindle occurrence.

In summary, given the well investigated role of sleep in memory consolidation surprisingly little is known about sleep effects on temporal order in episodic memories. In this study we therefore focused on the effect of sleep on (emotional) episodic stories using a sleep group and a sleep deprivation group. As it is well known that SWS enhances declarative memory consolidation and REM sleep is specifically beneficial for emotional content, an overall advantage in memory performance was expected for the sleep group. In the analyses we further focused on fine-grained investigation of non-REM (NREM)/REM cycles, and sleep spindle related oscillatory EEG changes. As will be shown, no one single sleep stage or mechanism appears to support sleep-dependent temporal order consolidation in our task, but rather the orderly interplay of NREM/REM cycles and spindle-related α-oscillations.

2. Materials and methods

2.1. Subjects

34 volunteers (17 women) with a mean age of 23.5 years (SD: 1.76; range: 19–28) participated in the study. All subjects were students, non-smokers, right-handed and had no severe organic or mental illness. They were regular sleepers and reported no sleep (PSQI < 5, Buysse et al., 1989) or mood disorder (SAS < 36, Zung, 1971; SDS < 40, Zung, 1965). Participants were randomly assigned to a sleep ($n = 16$) or a sleep deprivation group ($n = 18$).

All participants underwent an initial psychometric examination including the D-MEQ (Horne and Ostberg, 1976) for discriminating between evening and morning types, the FPI-R (Freiburger Personality Inventory Revised) (Fahrenberg et al., 2001) for personality assessment, as well as the APM (Advanced Progressive Matrices) (Raven et al., 1998) and the WMS-R (Working Memory Scale Revised) (Wechsler, 1987) for assessing general cognitive and memory abilities, respectively. Furthermore, subjects reported their medical history and their usual sleep habits. Subjects assigned to the sleep group started with an adaptation night preceding the experimental learning night. To control for constant sleep–wake rhythms before and during the experimental period, participants had to fill in sleep diaries and report their nightly dreams. Before study participation all subjects signed an informed consent form.

2.2. Study design

Both groups had to learn 8 different memory sequences in the experimental night. Each sequence consisted of 12 pictures. After the encoding sessions subjects were tested for the temporal order of the pictures. Only after this first retrieval subjects were told to which group they would be assigned (sleep or sleep deprivation). Subjects in the sleep group went to bed 15–30 min after encoding and stayed in bed for the next 8 h. Subjects in the sleep deprivation group had to stay awake the whole night (8 h) and the following day. The Psychomotor Vigilance Test (Wilkinson and Houghton, 1982) was carried out every hour (8 times) during the night (Hoedlmoser et al., 2011). In between the tests, subjects were allowed to play cards and drink water or tea but it was forbidden to eat or drink caffeine containing beverages or turn on normal lights. Room temperature was constantly kept at 20–22 °C and lights were dimmed to a maximum of 10 lx.

Subjects in both groups were retested with the temporal order task tested in the morning (15–30 min after 8 h of sleep or deprivation). The last retrieval test was then done in the morning three days after the experimental night (72 h after the second, morning retrieval). Additionally a classic recognition task was performed on day three.

2.3. Memory tasks

To explore the episodic memory strength (i.e., temporal order) we implemented a modification of a sequence learning task already used by Kumaran and Maguire (2006). Therefore faces and objects were selected as stimuli (48 grayscale front-facing photographs of unfamiliar male and female faces obtained from the Stirling database http://pisc.psych.stir.ac.uk/ as well as 48 grayscale photographs of objects obtained from the software HEMERA Photo Objects©). All subjects were required to learn 8 sequences of pictures in total, consisting of 6 faces and 6 objects in each sequence. To control for the mnemonic strategies used, subjects were given a standardized instruction which requested them to create a personal story for each sequence in which they were personally involved. The goal then would be to simply remember the order of the 12 pictures. After a demonstration period using two semantically similar sequences (hobby–garden, hobby–car) four different types of themes (holiday, illness, crime and profession) were presented for episodic encoding.

One encoding phase included two sequences for a given theme (e.g. holiday–summer and holiday–winter). Each sequence was presented twice over the course of one encoding phase, with a retrieval test of sequential memory at the end of each encoding block. Each encoding phase started with a context-specific cue displayed for 3500 ms: 'Learn: Sequence 1: Holiday/Summer'. Next, in a sequence encoding block lasting 42 s in total, 6 faces and 6 objects were presented one after another, each for the duration of 3500 ms, in the center of the screen on a black background. After this, a central fixation cross was displayed for 8000 ms followed by a further cue (displayed for 3500 ms) indicating that a retrieval block would shortly occur: 'Test: order of faces and objects'.

Each retrieval block consisted of three trials: in each trial, four pictures were presented side by side in random positions. Thus, over the course of three trials constituting the sequence retrieval block, all 12 pictures that were presented in the preceding encoding block were seen again. The array of four pictures was then displayed for 6000 ms during which subjects were required to determine the relative order in which the pictures appeared in the preceding sequence. After those 6000 ms subjects were requested by the cue 'Now respond!' to order the pictures by using the numerical keys 1–4 (max. respond time was set to 12,000 ms).

The temporal order of pictures indicated by subjects using the keypad was scored as follows: each face or object was awarded one point if in the correct position in the sequence relative to each other picture in turn. Therefore subjects could get a maximum of 6 points for one trial and 18 points for a complete sequence. If the correct order was e.g. A C D B and the subject correctly pressed that order, he/she got 3 points for A, 2 points for C and 1 point for D (cf. Kumaran and Maguire, 2006).

In addition a recognition test was conducted on day 3. This test comprised twice 96 pictures, with an equal number of previously seen and unseen faces/objects. Subjects were required by button press to indicate whether the face/object was new or old and how certain they were about their judgment (1–3) (cf. Supplementary Table 1).

2.4. EEG recordings

The electroencephalogram (EEG) was recorded utilizing Synamps EEG amplifiers (NeuroScan Inc., El Paso, TX). All signals were filtered (0.10 Hz high-pass filter; 70 Hz low-pass filter; 50 Hz notch filter) and digitized online with 500 Hz sampling rate. 23 EEG channels (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), 1 bipolar vertical electrooculogram (EOG) channel to control for eye artifacts, 1 bipolar submental electromyogram (EMG) channel, 1 bipolar electrocardiogram (ECG) channel and 1 bipolar respiratory channel (chest wall movements) were placed. Electrodes were attached according to the international electrode (10-20) placement-system. During adaption nights, polysomnography (PSG) recording included 8 EEG, 4 EOG, 1 bipolar ECG, 3 unipolar EMG (submental and left/right tibialis), and 4 respiratory channels (nasal airflow, chest and abdominal wall movements, oxygen saturation). Sleep was automatically scored and visually checked according to standard criteria (Rechtschaffen and Kales, 1968) by the Siesta Group.

2.5. Sleep cycles

Sleep cycles were analyzed using Matlab 7.0.1 built scripts using the criteria from Mazzoni et al. (1999) specifying that NREM and REM sleep has to be longer than 2 min in order to be scored as a cycle. A NREM/REM cycle was defined as sequence of NREM and REM sleep not interrupted by a waking period longer than 2 min. REM epochs shorter than 2 min were included in the previous sleep stage. Similarly, a sequence of NREM stages interrupted by a period of wakefulness longer than 2 min was not considered part of a NREM/REM cycle. In addition we required a NREM/REM cycle to be longer than 30 min. To obtain changes over the night, we calculated a NREM/REM ratio for the first, second and last cycles as these data were present across all subjects.

2.6. Sleep spindles

Sleep spindles were detected automatically using the frontal (F3/F4) and central (C3/C4) electrodes, re-referenced to contralateral mastoids. Spindle detection was based on the following criteria: (1) 11–15-Hz band-pass filtering, (2) amplitude > 25 μV, (3) duration > 0.5 s, and (4) controlling for muscle (30–40 Hz) and/or alpha (8–12 Hz) artifacts (for details refer to Anderer et al., 2005). Concerning band-pass filtering, spindles were divided into a slow range (including spindles from 11 to

Table 1
Number of slow and fast sleep spindles across the detection electrodes.

	Slow spindles			Fast spindles		
	Mean	SD	Range	Mean	SD	Range
F3	974	558	293–2611	578	429	54–1726
F4	889	506	306–2181	569	445	63–1756
C3	563	438	84–1509	1080	689	122–2836
C4	466	327	45–1159	1003	752	94–3127

13 Hz) and fast range (from 13 to 15 Hz). The measure spindle activity (termed SpA) captures the duration as well as amplitude of identified spindles and thus reflects the activity or intensity of the spindle process (spindle activity = mean spindle duration × mean spindle amplitude). Sleep spindles were calculated separately for sleep stage S2 and slow wave sleep (SWS).

2.7. Spindle related spectral power

For the time-frequency decomposition of spindles we randomly chose 20% of all detected S2 slow and fast spindles. The total sleep spindle number is depicted in Table 1. Spindle-event-related synchronization/desynchronization (SRS/SRD) was defined as change of sleep spindle power occurring in a given band, relative to a reference interval (350–150 ms before spindle onset; cf. Fig. 1). Spindle-event-related time frequency analyses were done for 5-s epochs (2500 ms before to 2500 ms after spindle onset) and for a frequency range of 1–40 Hz over the whole night for chosen S2 spindles. Triggers for event-related spindle analysis were taken from both detected slow (11–13 Hz) as well as fast (13–15 Hz) spindles and separately at each recording site (F3, F4, C3, C4). For visualization we show percent change values (with reference to the 350–150 ms pre-stimulus baseline) of participants enhancing or non-enhancing their temporal order knowledge from retrieval 1 to retrieval 2. Analysis was performed using complex Morlet wavelet transformation ($c = 10$; 1 Hz frequency steps) as implemented in BrainVision Analyzer 2.0 (Brain Products, Munich) and focusing on the alpha frequency band (7.33–11.92 Hz).

2.8. Statistical analyses

Statistical analyses were performed using SPSS 18.0.0 software (SPSS Inc., Chicago, IL). The significance level was set to $p < 0.05$ and Greenhouse–Geisser correction was applied when necessary. For post hoc comparison paired-sample t-tests were performed. Changes in behavioral performance (mean retrieval 1, 2, 3) were evaluated by paired samples t-tests. Subjects in the sleeping condition were further grouped according to overnight memory performance. Subjects with better or equal memory performance after the experimental night (RET1–RET2) served as memory enhancers ($n = 7$), the other subjects as memory non-enhancers ($n = 9$).

For statistical sleep cycle analysis we utilized Spearman correlations as the NREM/REM ratios were ordinally scaled and not normally distributed. Due to outliers we had to exclude one subject for sleep cycle analyses. Differences in sleep spindles were evaluated by four-factor Analyses of Variances (ANOVAs) for repeated measures with the within-subject factors spindle TYPE (fast spindles, slow spindles), HEMISPHERE (left, right), FRONT/CENT (frontal electrodes [F3, F4], central electrodes [C3, C4]) and the between-subject factor ENHANCEMENT (memory enhancers, memory non-enhancers). Dependent measures were spindle number and spindle activity. ANOVAs were also performed with the between subject factor WMS+/− (subjects with generally higher or lower memory function), and APM+/− (subjects with generally higher or lower cognitive abilities using median splits).

To analyze phasic spindle power, relative SRS/SRD values (with pre-spindle baseline) of 3 post-stimulus time windows were chosen starting with spindle onset (0–400 ms, 400–800 ms, 800–1200 ms). For analysis of alpha power following spindle onset two-factor ANOVAs with the within-subject factor TIME (0–400 ms, 400–800 ms, 800–1200 ms) and the between-subject factor ENHANCEMENT were calculated on each of the four spindle detection electrodes (F3, F4, C3, C4). Note that in the following we will focus on interactions of interest including the between-subjects factors ENHANCEMENT, WMS+/−, or APM+/−.

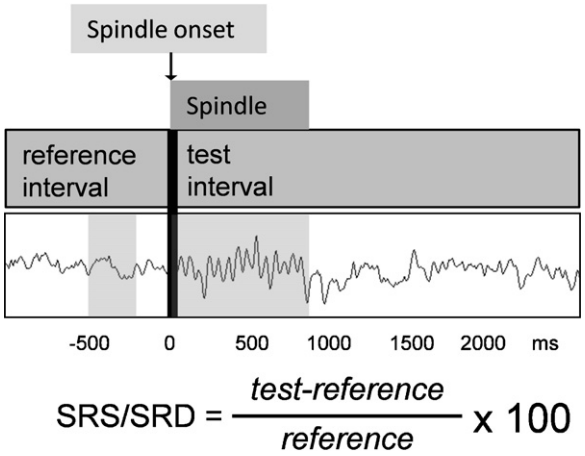

Fig. 1. Spindle-related-synchronization (SRS) and spindle-related-desynchronization (SRD). Note that the reference interval is a small time window before sleep spindle onset. The test interval is the area starting with spindle onset. Note that positive values indicate SRS.

Table 2
Memory retrieval scores and memory change scores for sleep and sleep deprivation group.

	Sleep group		Sleep deprivation group		
	Mean	SD	Mean	SD	p-Value (t-test)
Retrieval 1	16.13	1.55	16.50	0.75	0.373
Retrieval 2	15.81	1.55	15.23	1.33	0.249
Retrieval 3	14.66	1.73	14.09	1.67	0.331
RET2–RET1	−0.32	0.9	−1.27	0.89	0.004
RET3–RET1	−1.46	1.27	−2.41	1.30	0.039

For each of the two experimental groups (sleep, sleep deprivation) mean number of correct words is shown for all retrievals and their differences. p-Values indicate statistical differences between the two groups.

3. Results

3.1. Behavioral data

The performance data for temporal order memory are illustrated in Table 2. Interestingly, only the SDG group showed significant forgetting from retrieval 1 to retrieval 2 (SDG: $t_{18} = 6.013$, $p < 0.01$; SG: $t_{16} = 1.409$, $p > 0.05$; also see Supplementary Fig. 1A) whereas both groups significantly deteriorated in performance from retrieval 1 to retrieval 3 (SDG: $t_{18} = 7.862$, $p < 0.001$; SG: $t_{16} = 4.606$, $p < 0.001$). Due to the fact that the SDG group results of retrieval 2 are contaminated by fatigue (i.e., PVT reactions times significantly increase over the night: $F(7,119) = 10.271$, $p < 0.001$; cf. Supplementary Fig. 1B) we will focus on retrieval 1 to retrieval 3 changes in the following. See Hoedlmoser et al. (2011) for more detailed information including phase-locking changes during PVT across the sleep deprivation night.

Most importantly, present results indicate that sleep deprived participants perform worse in temporal order memory even if tested after three recovery nights ($t_{32} = 2.148$, $p = 0.039$; Fig. 2A) and although they exhibited identical arousal levels at retrieval 3 testing. Furthermore, observed memory change was unrelated to general memory ability (WMS-R Index; $r = 0.211$, $p = 0.231$) or abstract reasoning (APM) ($r = 0.091$, $p = 0.609$). With regard to our recognition test we did not observe any behavioral differences between the sleep and the sleep deprivation group ($t_{32} = 0.148$, $p = 0.476$).

3.2. Classical sleep measures and sleep cycles

As illustrated in Table 3 no overall differences in sleep architecture are present between the memory enhancers and non-enhancers of the sleeping group.

Concerning sleep cycle parameters, NREM/REM in the first cycle showed strong correlation with memory retention (RET3–RET1) ($r = -0.639$, $p = 0.010$) indicating that less (temporal order) forgetting of episodic memories over the three day period is related to a smaller NREM to REM ratio (i.e., more REM) in the first sleep cycle after learning. In addition the NREM to REM ratio in the first cycle was also correlated with general memory ability (WMS-R Index; $r = -0.589$, $p = 0.021$) with more REM relative to NREM

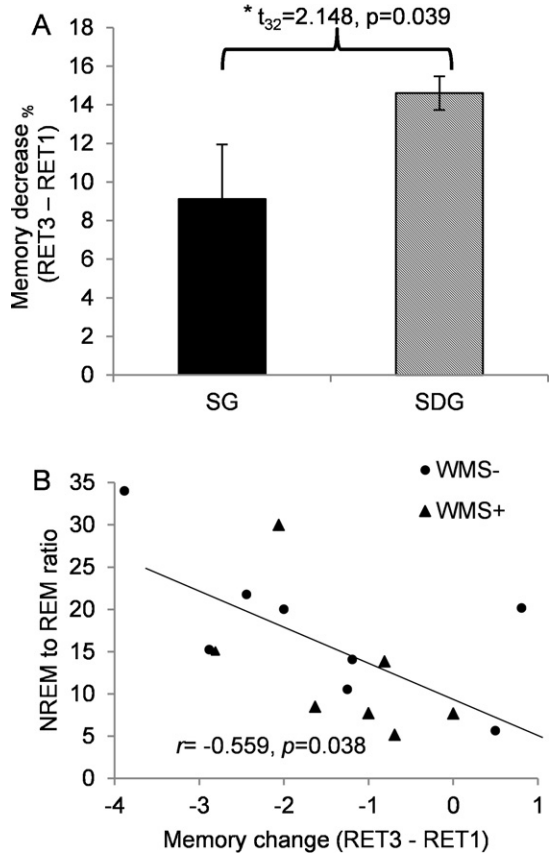

Fig. 2. Memory change and its interaction with NREM and REM sleep. (A) Subjects from the sleep group showed a significantly smaller decline in retrieval performance from initial temporal order recall (RET1) to delayed recall after 3 days (RET3) as compared to sleep-deprived subjects. (B) Depicted is the significant relationship of the NREM to REM ratio (staged 30 s epochs) and memory performance change (RET3–RET1). Note that the better the recall of temporal order of episodic memory over the three day period the more REM to NREM epochs in the first sleep cycle after learning. Data is controlled for influences of general memory ability (Wechsler Memory Scale, WMS).

in more "gifted" subjects. Controlling for the WMS "trait", partial correlation for NREM/REM and memory retention (RET3–RET1) still revealed unchanged significant results ($r = -0.559$, $p = 0.038$), therefore indicating a double association of NREM/REM ratios to memory and general cognitive ability (WMS). Fig. 2B represents the significant association of NREM/REM ratio and memory retention (RET3–RET1).

Neither the number of overall sleep cycles, mean cycle duration, total cycle time/total sleep time ratio nor later occurring sleep cycles revealed any further significant associations (cf. Supplementary Table 2).

Table 3
Descriptive statistics of sleep parameters and the differences between the memory enhancer vs. non-enhancer group.

	Enhancer		Non-enhancer		*p*-Value (*t*-test)
	Mean	SD	Mean	SD	
TST (min)	456.78	10.49	458.94	13.47	0.733
Sleep efficiency	94.40	2.21	95.46	2.13	0.345
Awakenings (*n*)	4.00	3.55	4.00	3.42	1.00
Wake (min)	5.57	5.75	5.61	6.22	0.990
Stage 1 (%)	3.62	1.46	4.74	1.53	0.164
Stage 2 (%)	48.49	7.14	51.36	7.42	0.447
SWS (%)	26.54	6.67	24.84	6.21	0.608
REM (%)	21.34	2.40	19.03	3.36	0.148

3.3. Sleep spindles

A four-way ANOVA for spindle numbers with repeated measures for spindle TYPE, HEMISPHERE, FRONT/CENT and between-subjects factor ENHANCEMENT revealed a significant main effect for HEMISPHERE ($F(1,16) = 9.619$, $p = 0.008$) indicating generally more spindles in the left hemisphere. The significant interaction TYPE × FRONT/CENT ($F(1,16) = 33.515$, $p < 0.001$) indicates more fast spindles on central regions and more slow spindles on frontal regions. An identical ANOVA for spindle activity also revealed a significant main effect for HEMISPHERE ($F(1,16) = 9.466$, $p = 0.008$) and significant interactions for TYPE × FRONT/CENT ($F(1,16) = 14.671$, $p = 0.002$) as well for TYPE × HEMISPHERE ($F(1,16) = 7.627$, $p = 0.015$) indicating stronger spindle activity on the left hemisphere and on frontal regions.

Consequently we selected the left hemispheric electrodes F3 and C3 for the following spindle-related analysis. Neither number nor activity of spindles correlated with general cognitive abilities in the present study.

The two-way ANOVA for fast F3 spindles and dependent measure alpha SRS/SRD power with repeated measures factor TIME and between-subject factor ENHANCEMENT revealed a significant main effect for factor ENHANCEMENT ($F(1,14) = 8.606$, $p = 0.011$) indicating more alpha power during fast spindles (0–1200 ms) for subjects who improved overnight (Fig. 3A). To reveal a more detailed picture, alpha power was correlated with overnight memory change and revealed a significant association in the 0–1200 ms ($r_{16} = 0.532$, $p = 0.034$) post-spindle onset time-window (Fig. 3B).

4. Discussion

Results indicate that temporal order in episodic memories is affected by sleep deprivation in the first night after learning. As the night after sleep deprivation is not representative for difference in memory consolidation due to fatigue effects we concentrated on memory performance change from initial learning to three days thereafter. Even after 3 recovery nights at home and identical arousal levels during follow-up testing the sleep deprived group performed worse in our emotionally laden temporal order task. The beneficial memory effect of sleep is well in line with other sleep deprivation studies (e.g. Drosopoulos et al., 2007; Stickgold, 2005) although temporal order in complex episodic memories had not been explicitly addressed before. Our results therefore extend the sleep-dependent memory consolidation hypothesis and once again pin point that the association is far from being simple. Our results point to the importance of various sleep mechanisms such as sleep spindle-related alpha power or NREM–REM ratios rather than supporting classical dual-process or dual-step models of sleep-dependent memory consolidation.

Whereas some studies divide the night in quarters for further analyses (e.g. Stickgold et al., 2000) only a few divide sleep into actual sleep cycles (e.g. Ficca et al., 2000). Although we could not replicate earlier findings from Ficca et al. (2000) reporting an association of sleep cycle number and memory improvement we did find a more fine-grained difference in the NREM/REM ratios. Interestingly we found that the exact balance of NREM to REM epochs in the first sleep cycle plays an important role for effective episodic long-term retention (cf. Fig. 2B). Specifically the more REM to NREM epochs in the first sleep cycle the better the memory performance 84 h after encoding. It appears that specifically 'early' parts of the night following learning have a crucial impact on sleep-dependent memory consolidation as various groups have earlier demonstrated (Gais et al., 2000; Huber et al., 2004; Marshall et al., 2006).

In accordance with this, Rauchs et al. (2004) discuss that especially a surplus of REM appears to counteract forgetting of

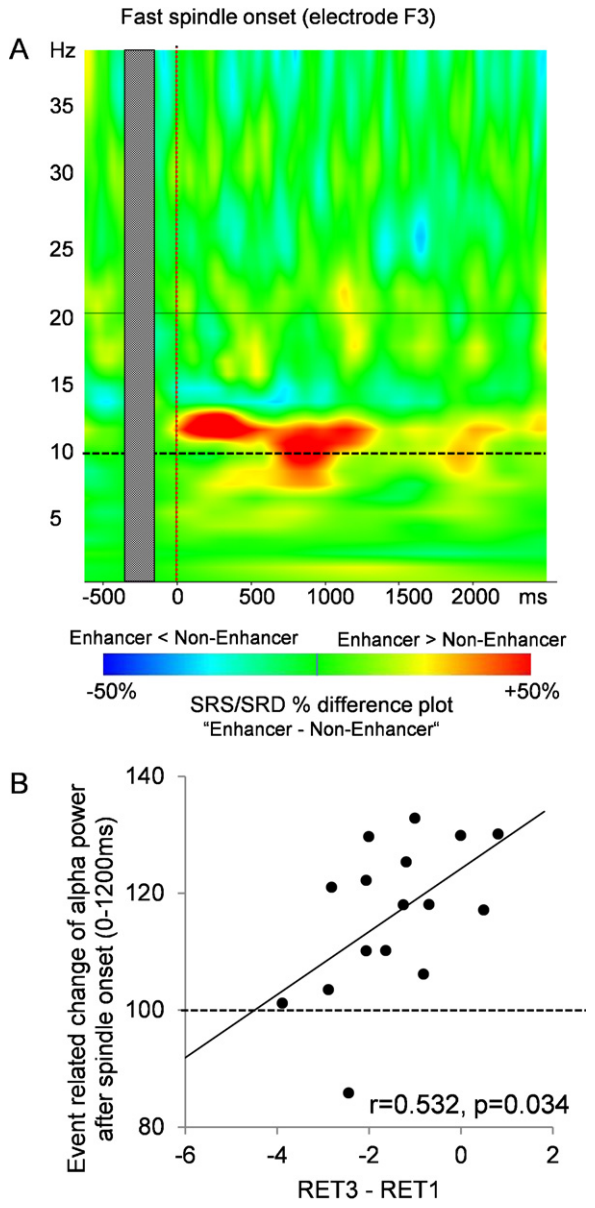

Fig. 3. Overnight memory change and its relation to spindle-related alpha synchronization. (A) The upper panel depicts the difference plot (enhancer minus non-enhancers) of fast spindle-event-related synchronization/desynchronization (SRS/SRD) at frontal recording site F3 in relation to a pre-spindle reference period (−350 to −150 ms; checkerboard shading). Note that "memory enhancers" show more alpha power 0–1200 ms after fast spindle occurrence. Hot colors indicate more SRS for "memory enhancers". (B) The lower panel depicts the corresponding correlation of spindle-related alpha power with overnight memory change 0–1200 ms after (fast) spindle onset (electrode F3).

emotional episodic memories. As also subjects in our study had to learn diverse emotionally laden stories related to "real world" content our memory task can be discussed in this light. Therefore and in line with the literature (for review see Diekelmann et al., 2009), we speculate that successful encoding or consolidation of emotionally laden temporal order in episodic memory depends upon a delicate balance of REM to NREM sleep epochs soon after falling asleep. A structured dialogue of NREM and REM processes might thereby support memory consolidation of various kinds; in the case of our specific task (i) numerous REM to NREM epochs early in the night (cf. Fig. 2) as well as (ii) fast-spindle related alpha oscillations in the frontal cortex (cf. Fig. 3) appear beneficial.

With respect to the latter, our data also indicated an unexpected left hemispheric preponderance in spindle number and spindle activity post-learning. Although speculative, this result is in line with the idea, that emotionally laden verbal information is more likely to be processed in left frontal cortical regions (Sergerie et al., 2005). Moreover, the hemispheric encoding/retrieval asymmetry model (HERA) (Habib et al., 2003) also suggests more involvement of the left hemisphere in episodic encoding which, in this case, may be reflected by sleep spindle activity.

A puzzling new finding in our study is the association of spindle-triggered EEG changes and memory change overnight. Interestingly it seems that the suspected "replay" does not necessarily have to occur in the spindle-specific frequency band but in related frequency bands time-locked to the occurrence of spindles. In our case the subjects who forgot less temporal information did show more spindle-related alpha band power at frontal electrode sites (cf. Fig. 3A). Yordanova et al. (2011) have already shown that alpha power, but only in slow wave sleep, is related to the transformation from implicit to explicit knowledge in a "number reduction task". With respect to the significance of alpha power we want to draw attention to earlier findings showing that alpha is closely associated with declarative memory performance (for reviews see e.g. Klimesch, 1999).

Good memory performance is usually characterized by a large event-related synchronization (ERS) during a period preceding a task and at the same time by a large event-related desynchronization (ERD) during actual task performance. This effect can even be enhanced by external rTMS stimulation in the pre-stimulus period (Klimesch et al., 2003). The findings obtained in the present study, however, indicate that a decrease in pre-spindle alpha power and a post-spindle increase is associated with good performance. Thus, when considering the onset of a spindle as an event during which information is retrieved from memory, our findings are exactly opposite to those that were found in retrieval tasks.

Yet, another alpha phenomenon may account for the observed effect. Specifically we found earlier that a memory relevant stimulus may also evoke a transient increase in alpha (cf. Klimesch et al., 2004) which was related to controlled access to memory with subsequent ERD reflecting conscious retrieval of that information (cf. Jaspers et al., 2010). Thus, we speculate that the transient increase in alpha power after spindle onset for memory enhancers may reflect access to the stored memory traces which enables re-activation and consolidation of the accessed information. Well in line with this interpretation of "offline memory access" is the fact that the discussed spindle-related alpha effect is only evident frontally.

In conclusion, the findings of the present study demonstrate the beneficial role of sleep in the temporal order of episodic memories. In fact, compared with the sleep deprived group, the sleep group showed better memory retention three days after encoding. Importantly, a well-ordered balance of REM to NREM epochs in the first sleep cycle as well as fast sleep spindles at frontal electrode sites appears to support memory formation of temporal aspects in episodic memories. Moreover we speculate that cortical "replay" is only marked by the sleep spindle, with the relevant activity occurring simultaneously in the alpha band reflecting "offline memory access and retrieval" of yet to be consolidated memory traces.

Conflict of interest

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.biopsycho.2012.05.012.

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