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Stimulation of the Brain With Radiofrequency Electromagnetic Field Pulses Affects Sleep-Dependent Performance Improvement

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ABSTRACT

Background: Sleep-dependent performance improvements seem to be closely related to sleep spindles (12–15 Hz) and sleep slow-wave activity (SWA, 0.75–4.5 Hz). Pulse-modulated radiofrequency electromagnetic fields (RF EMF, carrier frequency 900 MHz) are capable to modulate these electroencephalographic (EEG) characteristics of sleep.
Objective: The aim of our study was to explore possible mechanisms how RF EMF affect cortical activity during sleep and to test whether such effects on cortical activity during sleep interact with sleep-dependent performance changes.
Methods: Sixteen male subjects underwent 2 experimental nights, one of them with all-night 0.25–0.8 Hz pulsed RF EMF exposure. All-night EEG was recorded. To investigate RF EMF induced changes in overnight performance improvement, subjects were trained for both nights on a motor task in the evening and the morning.
Results: We obtained good sleep quality in all subjects under both conditions (mean sleep efficiency $> 90\%$). After pulsed RF EMF we found increased SWA during exposure to pulse-modulated RF EMF compared to sham exposure ($P < 0.05$) toward the end of the sleep period. Spindle activity was not affected. Moreover, subjects showed an increased RF EMF burst-related response in the SWA range, indicated by an increase in event-related EEG spectral power and phase changes in the SWA range. Notably, during exposure, sleep-dependent performance improvement in the motor sequence task was reduced compared to the sham condition (−20.1%, $P = 0.03$).
Conclusion: The changes in the time course of SWA during the exposure night may reflect an interaction of RF EMF with the renormalization of cortical excitability during sleep, with a negative impact on sleep-dependent performance improvement.

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Introduction

Large public and occupational populations are exposed to radiofrequency electromagnetic fields (RF EMF) as those emitted by mobile phones. Since these fields are mainly absorbed by the head, numerous studies investigated the effect of RF EMF exposure on brain physiology. Indeed, several studies consistently showed that RF EMF can alter brain activity. For example, studies focusing on electroencephalographical (EEG) spectral power showed that pulse-modulated RF EMF exposure increased power in the alpha and spindle frequency range (7.5–14.5 Hz) during non-rapid eye movement (NREM) sleep [1–6]. Recently, also an increase of delta power (<4.5 Hz) was observed [5]. Similarly, exposure during wakefulness increased alpha power in the spontaneous waking EEG (8–12 Hz, [7–9]). The crucial factor for these effects is the extremely low-frequency (<300 Hz) pulse modulation of the RF EMF, since exposure to the RF carrier frequency alone had no effect [7,8]. Thus, RF EMF pulses affect brain activity but do they

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also have an impact on daily performance? Indeed, though not very consistently, studies found performance changes after or during pulsed RF EMF exposure [10]. All of these studies investigated the effects of RF EMF exposure during wakefulness on performance. Since various studies support a crucial role of sleep in memory and learning processes (for a review see Ref. [11]) the question arises whether the RF EMF induced changes of brain activity during sleep may interact with these processes. Interestingly, the beneficial effects of sleep on post-sleep performance in specific learning tasks are closely related to sleep spindles (e.g., [12,13]) and to sleep slow-wave activity (SWA, EEG power between 0.75 and 4.5 Hz; (e.g., [14–16]). Since we have profound knowledge about how sleep spindles and slow waves are generated and regulated, we took advantage of this knowledge to study changes in brain activity during sleep. Slow waves are the main characteristic of deep sleep and visible as high-amplitude, low-frequency oscillations in the EEG [17]. They have a cortical origin and are closely related to the homeostatic regulation of sleep [18]. Thus, as sleep pressure dissipates in the course of a sleep period also SWA decreases [18]. Sleep spindles are generated by the thalamocortical system [19,20] and can be observed across the scalp (i.e., in different surface EEG derivations placed all over the scalp). Both sleep rhythms are involved in learning and memory processes and may be manipulated by pulsed RF EMF. We took advantage of these observations and aimed at 1) exploring possible mechanisms how pulsed RF EMF may affect cortical activity during sleep and 2) whether these effects on cortical activity during sleep interact with sleep-dependent performance changes. To do so, in our experiment each subject was exposed to RF EMF pulses during the sleep episode in one of 2 experimental nights. Our intermittent pulse modulation design of the RF EMF allowed us to investigate whether single RF EMF bursts directly evoke EEG responses during sleep. We further investigated whether pulse-modulated RF EMF during sleep interact with the reported sleep-dependent performance improvement in a well-characterized motor sequence learning task (e.g., [21]).

Materials and methods

Subjects

Sixteen healthy male subjects (18–21 years, 19.9 ± 0.2, mean ± SEM) participated and completed the study. The number of subjects was chosen based on previous studies that also investigated the effects of pulsed RF EMF and showed significant changes in spectral power in the sleep EEG (e.g., 1, 4, 8). Only male subjects were included since in female subjects spindle activity varied systematically across the menstrual cycle [22]. Participants underwent a telephone and questionnaire screening to exclude personal or family history of psychopathology, chronic diseases, sleep disorders, and current use of psychoactive agents or other medications. No subject traveled across more than 1 time zone 2 months before the start of the study. Subjects were right handed, non-smokers, free of sleep complaints, drugs, medication and were moderate mobile phone user (use < 2 h/week, 44.1 ± 9.0 min). They had to adhere to regular bedtimes (8 h time in bed, according to scheduled bedtime in the lab) 1 week before the experimental nights and abstain from caffeine, naps, and alcohol 3 days prior to the study nights. Compliance was controlled by breath alcohol test, wrist-worn actometers and sleep logs. During the day of the study night, physical exercise and the use of mobile phones were prohibited. The Cantonal Ethic Commission in Zurich (Switzerland) approved the study and written informed consent was obtained from all participants.

Procedure

In a randomized, double-blind, crossover design, each subject had 2 experimental nights with EEG recordings, one of them with all-night pulse-modulated RF EMF exposure (field study). An adaptation night was scheduled prior to each experimental night. Time in bed was 8 h for all subjects and all nights. Bedtimes were adjusted to the subject's preference and ranged from 22:00–24:00 to 06:00–08:00. For both experimental nights, subjects were trained on a motor sequence tapping task in the evening right before they went to bed. In the morning they were retested on the task to assess sleep-dependent performance improvement (e.g., [21]).

Exposure setup

During the whole sleep episode, the subject's head was exposed to RF EMF using a circular-polarized antenna facing down toward the volunteer's forehead (see Fig. S1 in Supplementary material for details about the exposure setup).

The 900 MHz RF signal was pulsed, with 7 consecutive 7.1 ms pulses forming one 500 ms burst. These 500 ms bursts were repeated every 4 s (Intermittent-1 phase, 0.25 Hz, corresponding approximately to occurrence of sleep spindles), and every 1.25 s (Intermittent-2 phase, 0.8 Hz, corresponding approximately to frequency of slow oscillations), respectively. Exposure of 5 min Intermittent-1 was followed by 1 min with no exposure (OFF phase), then 5 min Intermittent-2 was followed by a 7 min OFF phase. This 18 min sequence was repeated throughout the night.

The peak spatial specific absorption rate averaged over any 10 g tissue (psSAR10 g) during the 7.1 ms pulses was set to 10 W/kg. This resulted in a burst average of 1.0 W/kg. The whole night psSAR10 g averaged to 0.15 W/kg. A detailed description of the exposure setup and the dosimetric exposure assessment is given in the Supplementary material.

EEG recordings

EEG channels (10–20-system, F3, F4, C3, C4, P3, P4, O1, O2, A1, A2, referenced to vertex Cz), submental electromyogram (EMG) and vertical electrooculogram (EOG) were continuously recorded during the 8-h nighttime sleep period. The signals were recorded with a polygraphic amplifier Artisan (Micromed, Mogliano, Veneto, Italy), digitized at 1024 Hz (0.16–270 Hz) and transmitted via fiber-optic cables to a computer, running the software REMbrandt DataLab (Version 8.0; Embla Systems, Broomfield, CO, USA). The EEG signals were re-referenced to the mastoids (A1, A2) and filtered (0.5 Hz high-pass filter and 50 Hz low-pass filter). The sleep stages were scored for 20-s epochs according to standard criteria [23].

Artefacts were identified on a 20-s basis by visual inspection and with a semi-automatic procedure [2].

During sleep we undergo a characteristic sequence of NREM and rapid eye movement (REM) sleep with a period of approximately 90–100 min. This cyclic alternation of NREM and REM sleep is a basic feature of sleep. NREM and REM sleep episodes were defined according to standard criteria [24,25] and adapted when skipped REM sleep episodes were observed (6 of 32 nights, 4 subjects). In this case, we subdivided the first cycle manually (for details see Ref. [26]).

The first 4 NREM and REM sleep episodes were analyzed. All participants had at least 4 NREM and REM sleep episodes. In each subject, the minimal common number of 20-s epochs in the 2 conditions was analyzed in each NREM and REM sleep episode.

Spectral analysis

Spectral power of consecutive 20-s epochs was computed using a Fast Fourier routine (Hanning window, average of five 4 s epochs, frequency resolution 0.25 Hz). We used the C4A1 referential derivation for spectral analysis and for event-related responses because previous studies mainly found RF EMF induced effects in sleep EEG over central derivations (e.g., [1,5,6]). Frequencies between 0.75 and 15 Hz were analyzed. SWA was calculated as the spectral EEG power between 0.75 and 4.5 Hz. The initial REM sleep episode was only considered for analysis, when at least 3 min REM sleep occurred ($n = 10$). The relative decrease of SWA across night was defined as the SWA difference between the NREM episode expressing the maximal SWA and the NREM episode expressing the minimal SWA (episode number average: sham, 3.68; field, 3.5; Wilcoxon signed rank $P > 0.5$) relative to the episode with maximal SWA (sham, 1; field, 1.06; Wilcoxon signed rank $P > 0.5$).

Event-related spectral power (ERSP) and inter-trial coherence (ITC)

ERSP and ITC are methods of time-frequency analysis classically used to assess power (ERSP) and phase (ITC) changes across single trials time-locked to experimental events [27]. Synchronization in specific frequency bands indicates an induced activity due to an event (e.g., [28]). To establish how our specific RF EMF bursts lead to changes in EEG spectral power we performed ERSP and ITC in the NREM episode and frequency range that was significantly affected by exposure. We therefore compared ERSP and ITC of sham bursts and real Intermittent-1 phase bursts using the EEGLAB toolbox [27]. Furthermore, ERSP and ITC were calculated for the first and the second half of bursts within the significantly affected NREM sleep episode to assess the time course of the effect. Only the Intermittent-1 phase bursts provided enough data (4 s between bursts) to perform this analysis. For both conditions, only bursts during artifact-free epochs of the 4th NREM sleep episode were included in the analysis (referential derivation C4A1).

ERSP is an analysis that calculates the EEG power spectrum (short-time Fourier transform using 185 Hanning windows of 1024 data points (1 s)) time-locked to the RF EMF bursts. This time course of EEG power is next averaged across all RF EMF bursts [27,29]. ITC, also termed "phase-locking factor" [30], quantifies the phase consistency of activity in a specific frequency range across single trials time-locked to a stimulus, i.e., the RF EMF bursts. Thus, the higher the ITC value the higher is the synchronization between EEG data and the time-locking RF EMF bursts (i.e., EEG phase reproducibility across trials at a given latency; [27,31]). We used the same window parameters as for the ERSP analysis.

The EEG signal was band pass-filtered (0.5–5 Hz). Thereafter, the ERSP and ITC were calculated for the first 3500 ms after the bursts for the frequency range between 1 and 4 Hz (1-Hz resolution). Only artifact-free trials were included. Since we could not use a pre-event baseline (baseline was affected by bursts itself), we compared the ERSP and ITC between RF EMF bursts and sham bursts (trigger signal at similar time points as RF EMF bursts during the sham night) to asses RF EMF induced power and phase-locking changes.

Motor performance

A finger sequence tapping task before and after sleep was performed to assess motor performance. This task was adapted from Walker et al. [21]. Parallel versions were used in a balanced and randomized order for the 2 experimental sessions. This task required subjects to repeatedly complete, with their left hand, a five-element sequence (sequence 4–3–2–1–4 or 2–3–1–4–2; 1 is the digit finger) as fast and accurately as possible on a keyboard. The training before sleep consisted of twelve 30-s trials with 30-s breaks between the trials. During retest they performed 3 30-s trials interspersed with 30-s breaks. The sequence was continuously presented on the screen to prevent a working memory component and no feedback on pressing keys or about their performance was given. A keyboard (DirectIN keyboard, Empirisoft, New York) with a millisecond accuracy to measure response times (RT) between key-presses was used. Performance improvement in motor tasks are reflected in an increase of speed and a decrease of variability. Earlier studies exclusively investigated speed (as assessed by number of correct key-presses per time or mean RT) to investigate the consolidating role of sleep on performance (e.g., [21]). However, more recent studies question this sleep-dependent improvement in speed because it is also seen after 5 min wake and may depend on a decrease in fatigue [32,33]. We therefore focussed on the variability of the RT between key-presses to assess sleep-dependent performance improvement since there is evidence that sleep might reduce variability in a motor task [16]. Moreover, such a decrease of variability due to sleep in a visuomotor adaptation task seems to be closely related to sleep SWA [16]. This study further showed that additional learning after a training session did not improve variability, but a night of sleep did. We calculated the variance of RT to assess variability between the correct key-presses for each trial. Post-training performance was defined as the mean of the last 2 trials in the training session and retrieval performance as the mean of the first 2 trials during retest according to literature (e.g., [21]). Sleep-dependent performance improvement of variability was specified by the relative difference between the evening post-training and morning retrieval performance (%, [(retrieval performance − post-training performance)/post-training performance]).

To exclude possible confounding effects on performance we compared different subjective measures for both conditions. To do so, prior to each motor learning task subjects were asked about their alertness and mood (assessed by a 6 item visual analog scale) and in the morning subjective sleep quality was assessed by a questionnaire. Subjects' answers did not differ between the conditions (all $P > 0.15$). Subjects did not perceive the field since their answers were below chance level.

Statistics

Spectral power changes were analyzed using 2-way repeated-measures ANOVA with the 2 within subject factors 'condition' (field vs. sham) and 'sleep episode' (1st–4th NREM sleep episode). Absolute EEG spectral power data was log transformed prior to testing to approximate normal distribution. To quantify differences in the SWA time course between field and sham condition post hoc 2-tailed paired *t*-test were applied.

The difference in the ERSP and ITC in the SWA range between the field exposure and sham night was obtained using 2-tailed paired *t*-tests for each time point after the pulse.

Sleep-dependent performance improvement difference between the 2 conditions was analyzed with a repeated-measures analysis of covariance (ANCOVA) with the factor condition (field vs. sham) covarying for post-training performance difference (baseline difference). Correlations of performance and SWA were obtained using Pearson correlation.

Results

Minor effects of RF EMF exposure on sleep architecture

In a first step, we quantified the RF EMF effects on sleep architecture (see Table S1 in Supplementary material). Only minor

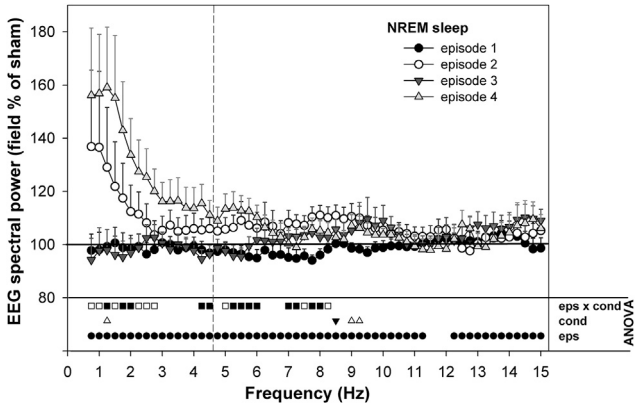

Figure 1. EEG power density of the field night as a percentage of the sham night (100%, solid black horizontal line) for the first 4 NREM sleep episodes (mean + SEM). Frequencies were analyzed between 0.75 and 15 Hz (0.25 Hz resolution). Lower panel of the figure shows results of the 2-way repeated-measures ANOVA (episode [eps]: 1st–4th NREM episode; condition [cond]: field vs. sham and their interaction [eps × cond]). Filled black symbols in the lower panel indicate significance ($P < 0.05$) and open symbols trends ($P < 0.1$). Vertical gray dashed line delineates the end of the SWA range (0.75–4.5 Hz). Post hoc paired *t*-test revealed significant differences in the SWA range bins only for the 4th NREM sleep episode.

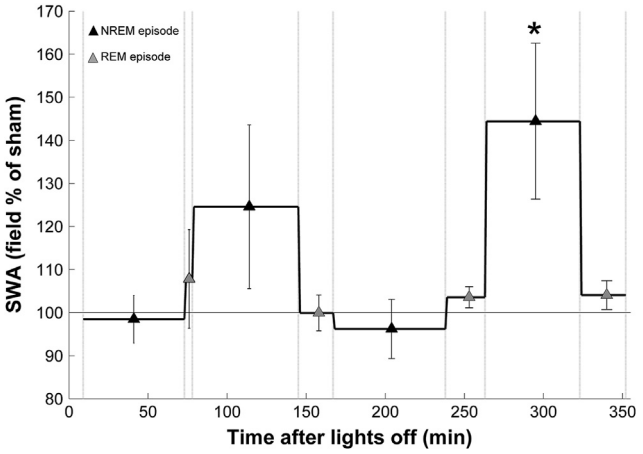

Figure 2. Time course of slow-wave activity (SWA; 0.75–4.5 Hz) during RF EMF exposure as a percentage of the corresponding sham condition for the first 4 NREM and REM sleep episodes ($n = 16$, mean ± SEM). Black and gray triangles indicate NREM and REM sleep episodes, respectively. Gray vertical lines delineate the average beginning and end of NREM and REM sleep episodes. The first REM sleep episode includes data of 10 subjects only. The star indicates a significant difference between sham and field exposure ($P < 0.05$, paired *t*-test).

changes were observed. Subjects during exposure showed a 2.1% decrease of total sleep time (−9.23 ± 3.40 min, mean ± SEM; $t = -2.31$, $P = 0.04$) and, as a consequence, exhibited reduced sleep efficiency (−1.92 ± 0.83%; $t = -2.31$, $P = 0.04$). This reduction was primarily due to an increase of wake after sleep onset (6.63 ± 2.60 min; $t = 2.55$, $P = 0.03$). NREM and REM sleep episode duration did not differ between the 2 conditions (all $P > 0.1$).

RF EMF changed EEG spectral power during NREM sleep

Field exposure induced an NREM sleep episode specific increase in spectral power in the low-frequency range. Frequencies up to 10 Hz were affected by exposure (Fig. 1). Looking at the relative change (% increase), the strongest effects were observed in the SWA frequency range. Thus, for further analysis we focused on SWA since it also reflects the major characteristic of deep NREM sleep, which was shown to be related to sleep-dependent performance changes [15,16,34]. Characteristically, SWA decreases in the course of sleep, reflecting the recuperative function of sleep [18]. To assess changes in the time course of SWA, we calculated average SWA in each NREM sleep episode. During both conditions SWA decreased in the course of the night. However, we found higher SWA in the 4th NREM sleep episode compared to the sham exposure ($P < 0.05$, Fig. 2) and thus, the decrease of SWA from the 1st to the 4th NREM sleep episode tended to be less pronounced during exposure ($P = 0.07$). No other NREM or REM sleep episodes revealed significant differences between the conditions (all $P > 0.25$).

Induction of SWA by pulsed RF EMF

Given this SWA enhancement toward the end of sleep, we further analyzed the EEG of the 4th NREM sleep episode during exposure to test whether single RF EMF bursts may lead to an event-related response in the SWA range. Thus, we investigated whether the increase in SWA is related to phase-locking, i.e., reflected in ITC, or amplitude changes, i.e., reflected in ERSP. RF EMF bursts increased ERSP in the SWA frequency range for several time points in the inter-burst interval mainly for the first half of the bursts (Fig. 3A). In addition, we found that RF EMF bursts increased phase-locking of the EEG signal in the SWA frequency range at around 2300–2500 ms after the burst both, in the first and second half of the bursts (Fig. 3B). These findings suggest an RF EMF burst-related increased phase-locking and synchronization in the SWA range in specific time windows after the RF EMF bursts and therefore indicate an induction of SWA due to pulsed RF EMF exposure. SWA in NREM sleep episodes 1–3 did not show a significant increase in ERSP and ITC after RF EMF bursts.

RF EMF exposure affected sleep-dependent motor performance improvement

Subjects significantly improved their performance quality, as assessed by the reduced variance of the RT, from evening to morning during sham (49.04 ± 6.40% reduction, $P < 0.05$) and exposure (28.97 ± 10.69%, $P < 0.02$). The baseline values in the evening did not differ between the field and sham condition (field: 24,270.3 ms ± 7166.9 ms; sham: 23,581.8 ms ± 6414.3 ms; $P > 0.8$). Thus, learning was comparable between the 2 conditions. However, sleep-dependent performance improvement was reduced during exposure compared to the sham condition (−20.08 ± 10.57%, Greenhouse–Geisser $F = 5.76$, $P = 0.03$). In a next step, we explored the relationship between the recuperative function of sleep, as measured by the decrease of SWA across the night, and sleep-dependent performance improvement. We found a positive correlation between the sleep-dependent performance improvement (variance of RT) and the decrease of SWA during the sham night ($r = 0.63$, $P < 0.01$). No significant correlation was present during the exposure night ($r = 0.27$, $P > 0.3$). To test whether the increased SWA in the 4th NREM sleep episode observed under field exposure might be related to the reduced sleep-dependent performance improvement we correlated SWA in the 4th NREM sleep episode with post-sleep performance improvement. This analysis showed that indeed higher SWA in the 4th NREM sleep episode was related to a reduced sleep-dependent performance improvement in RT variance ($r = -0.59$, $P = 0.02$) in the sham condition. Again, no significant correlation was observed for the active field condition ($r = -0.21$, $P > 0.4$). Moreover, we found a trend that a larger increase of SWA from sham to field condition in the 4th NREM sleep episode was reflected in a larger

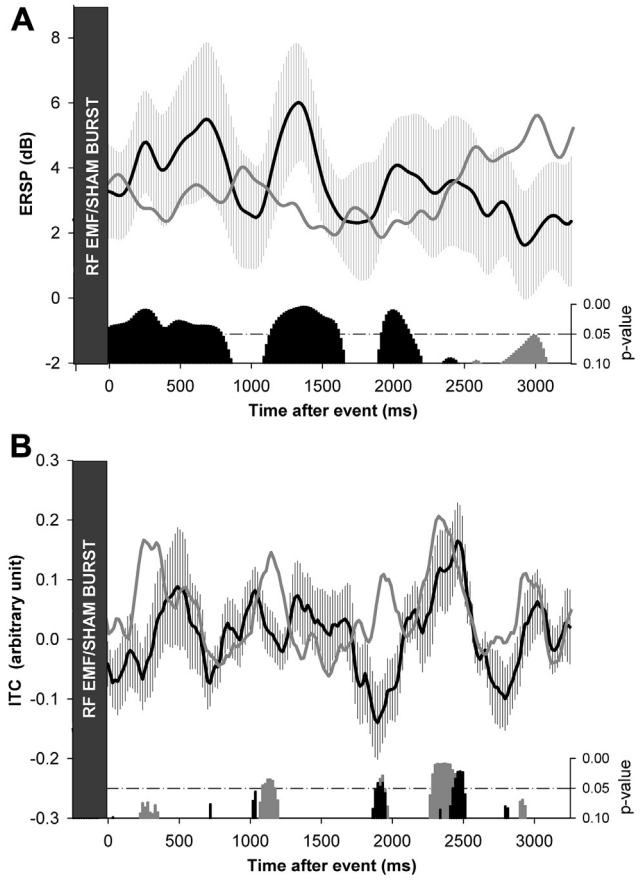

Figure 3. Event-related responses (ERSP and ITC) in the SWA frequency range during exposure compared to sham in the 4th NREM sleep episode. 'Event' indicates RF EMF bursts (field) or a corresponding trigger burst during the sham condition. Horizontal lines indicate the mean event-related response differences between the field and sham condition in the SWA frequency range (1–4 Hz) for the first half (black line) and second half of the bursts (gray line). Error bars indicate SEM of the first half of the bursts. Bars in the lower (statistic) panels illustrate *P*-values (≤0.1, black: first half of bursts, gray: second half of bursts). (A) Time course of the event-related spectral power (ERSP) after RF EMF bursts relative to sham bursts. (B) Time course of the inter-trial coherence (ITC, phase-locking) after RF EMF bursts relative to sham bursts.

reduction of sleep-dependent performance improvement from the sham to the field condition ($r = 0.47$, $P = 0.07$).

Discussion

In this study, we showed that very-low-frequency pulse-modulated RF EMF exposure resulted in increased SWA towards the end of the sleep period and reduced sleep-dependent motor performance improvement. Furthermore, we provide first evidence that the increased SWA results from a direct induction of sleep slow waves by RF EMF pulses.

Our data support the notion that changes in EEG activity during sleep due to RF EMF exposure are among the most robust effects EMF have on biological systems [35]. RF EMF exposure resulted in increased SWA compared to the sham condition. However, most previous studies reported effects in the spindle frequency range [1–6]. A possible explanation comes from a dose response study showing that pulsed RF EMF with average SAR levels equal or lower than 0.2 W/kg were not sufficient to significantly increase spindle activity in the sleep EEG [4], whereas exposure at SAR levels equal or above 1 W/kg showed a significant increase (e.g., 1, 4). Our average all-night SAR value was 0.15 W/kg, and the relevant 6 min average never exceeded 0.34 W/kg, and therefore, might be below the intensity that would lead to a significant increase in spindle activity. A recent study showing increased SWA during NREM sleep after 2-Hz pulse-modulated RF EMF exposure suggests that a prominent or principal pulse modulation in the delta range (<5 Hz) of the RF EMF might be needed to induce an increase in SWA during sleep [5]. Our bursts were presented in this low-frequency range (0.25/0.8 Hz).

We provide first evidence that single RF EMF bursts may affect sleep EEG activity by induction of SWA. However, potential mechanisms explaining how these fields may induce SWA are so far unknown. Using a special intermittent pulse modulation design of the RF EMF exposure we demonstrated that single RF EMF bursts may directly change EEG activity in the SWA range. This was demonstrated by the increased ERSP and by the increased phase coherence (ITC) in the SWA range after the RF EMF bursts. The results show that the effect in ERSP is most pronounced during the first half of the bursts and that significant effects in the ERSP and ITC are seen particularly during early time points during the inter-burst interval. We do see also late ERSP and ITC changes for which we have no good explanation. Our results suggest that RF EMF may be capable to directly induce or entrain EEG activity during sleep.

The question arises why the SWA increase was only significant toward the end of sleep. There is evidence that applied weak electrical fields can entrain spiking activity of neurons and synchronize them [36]. Thus our RF EMF may also entrain and synchronize neuronal activity in the SWA range. We have good evidence that the level of neuronal synchronization is a key feature determining the amplitude of slow waves, i.e., the level of SWA [37]. Thus, an entrainment of ongoing activity by field exposure may rely on a similar mechanistic explanation for the changes in SWA. At the beginning of the sleep period, neurons are almost perfectly synchronized, which is reflected in high values of SWA [38]. Thus, it seems to be plausible that at the beginning of sleep a weak RF EMF may not be able to further enhance synchronization of neural activity. However, toward the end of the sleep period the level of synchronization decreases [38] allowing RF EMF to exert their capability to enhance synchronization. A similar explanation may apply for our observation that increased ERSP in the SWA frequency range is most pronounced in the first half of the bursts. It is established that SWA shows a gradual build up during the initial phase of each NREM sleep episode [39] and as a result average SWA is at a lower level during the first half of the episode. Considering that the field may increase neuronal synchronization especially when SWA is less pronounced, we would expect a stronger effect on ESRP during this initial phase.

An ultimate cellular mechanism explaining this synchronization still remains elusive. Among others, we see 2 candidate mechanisms. First, inducing an event-related brain response may suggest that there is a receptor or an unknown human sensor that perceives RF EMF and causes oscillatory brain activity when exposed to such fields [40]. The second candidate mechanism is based on recent findings of Anastassiou et al. [41]. They introduce the concept of non-synaptic or ephaptic coupling of cortical neurons. In other words, EMF develops outside of neurons due to neuronal activity. These fields are not just a mere epiphenomenon of neuronal activity, but rather feedback onto neuronal activity. Even though these fields are very weak, they were able to strongly entrain and synchronize the spike-timing of the neurons. Considering that small changes of these endogenous fields could affect neuronal functioning, further investigations should explore whether pulse-modulated RF EMF interact with these endogenous fields.

Both candidate mechanisms might lead to changes in SWA as they are not mutually exclusive. Additional studies are needed

to explore such fundamental mechanisms for brain functioning. Our study shows that RF EMF can be used to explore such mechanisms. An interesting example for the usefulness of RF EMF exposure to study brain function is provided by our observation that the induced SWA is related to reduced sleep-dependent performance improvement.

Increasing evidence shows that SWA during NREM sleep is critically involved in the regulation of cortical excitability and synaptic strength across 24 h [38,42]. Thus, during waking cortical excitability increases through synaptic potentiation. During sleep a reduction of synaptic strength takes place, normalizing the increase in excitability observed during the day [38,42,43]. This reduction of synaptic strength is mirrored in SWA [42]. Therefore, the changes in the time course of SWA during the field night may reflect an interference of RF EMF with the normalization of cortical excitability during sleep. Consistent with previous research, low-frequency pulse-modulated RF EMF may affect cortical excitability [44]. Following field exposure Ferreri et al. [44] found increased intracortical facilitation measured with a paired pulse transcranial magnetic stimulation paradigm. This is up to now the most direct evidence that pulse-modulated RF EMF may directly affect cortical plasticity. There is evidence that slow waves might also causally affect and not just reflect synaptic strength [45]. Thus, the altered time course of SWA may result in an imbalance in the regulation of synaptic strength. The renormalization of synaptic strength during sleep showed beneficial effects of motor performance [16]. Since sleep-dependent improvement of motor performance was reduced under RF EMF exposure, our behavioral data further support the suggestion of an imbalance in the regulation of synaptic strength. We confirmed this finding since the decrease of SWA across the sham night correlated with sleep-dependent performance improvement. Thus, the more SWA in the 4th NREM sleep episode was increased during RF EMF exposure the more tended sleep-dependent performance improvement to deteriorate. Taken together, our findings suggest that the interaction of pulsed RF EMF with the regulation of synaptic strength may explain our behavioral results. We performed a single exposure and thus cannot exclude adaptation effects. As a consequence we cannot state anything about long-term effects. The large interindividual differences within our well-defined subject population clearly showed that our results cannot be generalized – other subpopulations may show opposite effects. Further studies are needed to investigate the cause of such large interindividual differences.

In summary, our study showed that RF EMF may directly affect ongoing brain activity during sleep, and as a consequence alter sleep-dependent performance improvement. RF EMF may therefore represent a non-invasive stimulation tool that is not consciously perceived for the manipulation of brain activity to study basic mechanisms of sleep and wake regulation, and performance behavior and may lead in the future to new therapeutic approaches.

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Supplementary material

Supplementary material related to this article can be found in the online version at http://dx.doi.org/10.1016/j.brs.2013.01.017.

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