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An experimental study on effects of radiofrequency electromagnetic fields on sleep in healthy elderly males and females: Gender matters!

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ABSTRACT

Background: Results from human experimental studies investigating possible effects of radiofrequency electromagnetic fields (RF-EMF) on sleep are heterogeneous. So far, there is no study on possible sex-differences in RF-EMF effects.

Objectives: The present study aimed at analyzing differences in RF-EMF effects on the macrostructure of sleep between healthy elderly males and females.

Methods: With a double-blind, randomized, sham-controlled cross-over design effects of two RF-EMF exposures (GSM900 and TETRA) on sleep were investigated in samples of 30 elderly healthy male and 30 healthy elderly female volunteers. Participants underwent each of the three exposure conditions on three occassions following an individually randomized order resulting in a total of nine study nights per participant. Exposure was delivered for 30 min prior to sleep and for the whole night (7.5 h) by a head worn antenna specifically designed for the projects. The peak spatial absorption rate averaged over time in head tissues (psSAR10g) was 6 W/kg for TETRA and 2 W/kg for GSM900. Thirty variables characterising the macrostructure of sleep and arousals as well as four subjective sleep variables were considered for statistical analyses.

Results: Multivariate analyses revealed that exposure to GSM900 and/or TETRA resulted in a significant reduction in arousals, a shorter latency to sleep stage N3, and a shorter self-reported time awake after sleep in both males and females. Exposure effects depending on sex (significant interactions) were observed. Latency to sleep stage R was shorter in females and tended to be longer in males under both exposures. Latency to stage N3 was shorter in females under TETRA exposure and almost not affected in males. The time awake within the sleep period under TETRA exposure was shorter in females and only slightly longer in males. Under GSM exposure, the self-rated total sleep time tended to be longer in females and to be shorter in males. Finally, the number of awakenings was lower only in females and tended to be higher in males under GSM exposure.

Discussion: With regard to RF-EMF effects on human sleep it seems that gender matters since GSM900 and TETRA led to significantly more exposure effects in females. Regardless of gender, none of the observed changes is indicative of a sleep disturbing effect of RF-EMF exposure. Observed effects might be mediated by skin related thermoregulatory mechanisms.

1. Introduction

Given the ubiquitous presence of mobile phones, base stations, cordless phones, smart meter, wireless networks at home and in public buildings, radio and/or television towers etc, there is concern in parts of the population that the radiofrequency electromagnetic fields (RF-EMF) emitted from these sources may have negative consequences for health.

One of the prominent complaints attributed to RF-EMF exposure from mobile phones and specifically base stations are sleep problems (TNS Opinion & Social, 2010). However, neither cross-sectional (e.g., Huss et al., 2015; Mohler et al., 2010) nor prospective epidemiological studies (e.g., Mohler et al., 2012) with an objective indicator of exposure could confirm an association between RF-EMF exposure and sleep.

An approach, which complements epidemiological studies, is to

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Table 1
Effects of RF-EMF exposure on the macrostructure of sleep in nine studies out of 20 that observed an effect in at least one variable. Δ indicates the direction of deviation under RF- EMF exposure from sham: ↑ = increase, ↓ = decrease; I indicates the interpretation of the observed deviation: + = beneficial for sleep, - = disadvantageous for sleep.

Author(s)	Δ	I	Sleep parameter[a]
Hung et al. (2007) [b]	↑	-	sleep onset latency
Mann & Röschke (1996)	↓	+	sleep onset latency
Loughran et al. (2005)	↓		stage R latency
Lowden et al. (2011)	↑		stage N3 latency
Lustenberger et al. (2013) [c]	↓	–	total sleep time
Lustenberger et al. (2013) [c]	↓	–	sleep efficiency index
Lustenberger et al. (2013) [c]	↑	-	wake after sleep onset
Borbély et al. (1999)	↓	+	wake after sleep onset
Lowden et al. (2011)	↑		stage N2
Danker-Hopfe et al. (2011)	↓		stage N2
Lowden et al. (2011)	↓	–	stage N3
Danker-Hopfe et al. (2011, 2016)	↑		stage R
Mann & Röschke (1996), Schmid et al. (2012b) [d]	↓		stage R
Danker-Hopfe et al. (2011)	↓	+	changes to stage N1

[a] Except for Lustenberger et al. (2013) and Danker-Hopfe et al. (2011, 2016) sleep analysis was performed according to the Rechtschaffen and Kales (1968) standard. Nevertheless, the AASM terminology (Iber et al., 2007) was used to describe to outcome variables, i.e. N1 instead of S1, N2 instead of S2, N3 instead of S3, S4, or slow wave sleep (SWS), R instead of REM.

[b] The only of the 20 studies which refers to a 90 min napping in the afternoon and not to a full night recording.

[c] Given a fixed time in bed, a decrease in total sleep time implies an increase in wake after sleep onset and a decrease of the sleep efficiency index.

[d] Only observed in the second sleep cycle.

investigate exposure from RF-EMF on sleep in human experimental settings. This has the advantages that a) exposure can be well controlled and b) that sleep can be measured by polysomnography (PSG) additionally to subjective assessments of sleep as a symptom. A limitation of experimental studies is that only short-term effects can be investigated.

In laboratory settings effects on measurable indicators of sleep quality - specifically sleep disturbing effects – so far have rarely been observed in human experimental studies. Table 1 briefly summarizes volunteer studies, which analysed effects of RF-EMF exposure on the macrostructure of sleep. Indicators of a disturbed sleep, among others, are: (1) an increased sleep onset latency (SOL; indicating problems to fall asleep), (2) less total sleep time (TST), (3) a prolonged wake time after sleep onset (WASO), (4) a higher number of awakenings, (5) more lighter sleep (stage N1), (6) less slow wave sleep (stage N3), which is the most restorative part of sleep, (7) more arousals from sleep, and (8) more frequent sleep stage changes.

Altogether, 20 studies looked at the macrostructure of sleep. Two studies investigated effects based on a daytime napping study (Huber et al., 2000; Hung et al., 2007) while all others considered night sleep. Eleven of them did not find an effect at all (Fritzer et al., 2007; Hinrichs et al., 2005; Huber et al., 2000; Huber et al., 2002; Loughran et al., 2012; Lustenberger et al., 2015; Nakatani-Enomoto et al., 2013; Regel et al., 2007; MR Schmid et al., 2012a; Wagner et al., 1998; Wagner et al., 2000). Nine found selective effects, which are, however, quite heterogeneous (Borbely et al., 1999; Danker-Hopfe et al., 2011; Danker-Hopfe et al., 2016; Hung et al., 2007; Loughran et al., 2005; Lowden et al., 2011; Lustenberger et al., 2013; Mann and Roschke, 1996; MR Schmid et al., 2012b). The 20 studies vary in several aspects, among others in the number of considered sleep variables, signal type, exposure duration, age and gender distribution of the sample. The majority of studies (n = 12) investigated subjects up to the age of 30, only two studies included males and females of broader age ranges (20–51 years and 18–60 years) (Loughran et al. 2005, 2012). For further details, see Danker-Hopfe et al. (2016).

So far, age and gender specific variations in studies on possible RF-EMF effects on sleep have not been considered. However, sleep parameters vary physiologically with age and gender (Hertenstein et al., 2018; Mitterling et al., 2015; Yetton et al., 2018). With regard to gender-specific variations Mitterling et al. (2015), who investigated a sample of 100 healthy participants covering the age range from < 30 years to > 60 years, oberserved statistically significant less stage N1 sleep and more stage N2 sleep [both as percent of the sleep period time (SPT)] in women as compared to men. Hertenstein et al. (2018) analysed data from 206 healthy subjects (121 women and 85 men) in the age range from 19 to 73 years. A linear regression with age and sex revealed a statistically significant sex effect for wake periods (women < men), stage N1 sleep (% of the SPT; women < men), and stage N3 sleep (% of the SPT; women > men). The study by Yetton et al. (2018) confirms that women have less stage N1 sleep (min) and more slow wave sleep (min) than men. The data regarding stage N2 sleep deviate from the results presented by Mitterling et al. (2015). According to Yetton et al. (2018) women have less stage N2 sleep (min) than men do. The figures shown in Yetton et al. (2018) seem to indicate that these sex differences increase with age. The sample sizes specifically in the group of elderly subjects, however, were too small in the studies by Mitterling et al. (2015) and Hertenstein et al. (2018) to look at gender differences by age groups.

The aim of the present study was to investigate whether effects of whole night RF-EMF exposure on sleep seen in a sample of elderly healthy females differ from results obtained from elderly healthy males, who were investigated with the same exposures, methodology and study design.

2. Methods and materials

2.1. Participants

The data used for the present analysis were collected in two different research projects with identical study designs. All experiments took place at the Competence Center for Sleep Medicine at the Charité – Universitätsmedizin Berlin (Table 2). Thirty healthy elderly females aged between 60 and 80 years were enrolled in study 1. The sample of study 2 included 30 healthy elderly males between the ages of 60 and 80 years. Participants of both studies were mainly recruited through flyer, electronic advertisements and word-of-mouth recommendation.

Table 2
Overview of RF-EMF studies considered in this paper. The exposure is expressed as 10 g peak spatial average specifc absorption rate ($psSAR_{10g}$).

Sample	Sex	n	Age (years) Mean ± SD Range	Exposure conditions	psSAR10g	Exposure duration
Sample 1	Female	30	67.8 ± 5.7 60–80	GSM 900 MHz TETRA SHAM	2.0 W/kg 6.0 W/kg –	7.5 h + 30 min prior to sleep
Sample 2	Males	30	69.1 ± 5.5 60–80	GSM 900 MHz TETRA SHAM	2.0 W/kg 6.0 W/kg –	7.5 h + 30 min prior to sleep

Both studies were conducted in accordance with the Declaration of Helsinki and the protocols were approved by the ethics committee of the Charité – Universiätsmedizin Berlin (EA4/122/13 for both studies). All particpants signed an informed consent and received a monetary compensation for their participation.

2.2. Screening

To be eligible for participation subjects had to pass four levels of screening (telephone interview, questionnaires, medical examination and screening nights in the sleep laboratory) to check inclusion and exclusion criteria, which are outlined in detail in Tables A1 and A.2, respectively, in the Appendix.

2.3. Design

Both studies were performed as randomized clinical trials, i.e. they were double-blind (neither the participants nor the experimenters were aware of the applied exposure condition), "placebo" (sham) controlled and designed as cross-over studies in which each participant received all exposure conditions in a randomized and counter-balanced order. The design of the two studies is summarized in Fig. 1a. Each participant spent ten nights in the sleep laboratory (including the screening night, which also served as an adaptation night to the laboratory environment). The nights were scheduled at time intervals of approximately two weeks to control for possible carry-over effects. Three different exposure conditions were applied three times in the following nine experimental nights. As depicted in Fig. 1b, subjects were exposed for the whole night (7h and 30 min). Additionally, they were exposed 30 min prior to sleep since several studies (e.g., Huber et al., 2002; Regel et al., 2007) have shown that an exposure prior to sleep has an impact on sleep, which is reflected in the spectral power of the electroencephalogram (EEG). Participants were instructed to keep a regular sleep-wake schedule for the duration of the study (i.e. bedtimes between 22:00 and 24:00 h), not to drink caffeinated beverages after 12 noon, and not to drink alcohol (controlled by a breathalyzer test upon arrival in the lab) at the days followed by an experimental night.

To control for a sequence effect randomization was realized in blocks. Each block (first three, second three and third three sessions) comprised each of the three exposure conditions exactly once. Sequences of exposure conditions within the three blocks did never repeat for one subject and were different between all subjects. All (six) possible sequences within blocks appeared at the same frequency. This type of randomization can be achieved with an even number of subjects. If subjects dropped out during measurements, precautions were necessary to keep the balancing. The software controlling the exposure system contained an approach to re-use randomization schemes of dropped out subjects.

Data collection for both studies took place over a period of about two years (females: December 2014 to September 2016; males: May 2016 to April 2018).

2.4. Exposure systems and dosimetry

Exposure consisted of generated signals that simulated Global System for Mobile Communications (GSM) and Terrestrial Trunked Radio (TETRA) exposures in addition to SHAM. RF-EMF exposures were delivered by systems specifically designed for each study comprising head worn antennas, feeding RF cables, signal generators, power amplifiers, measuring devices, as well as computer hardware and software for automatic control and monitoring of the experimental exposure in a double-blind manner. RF exposure was applied to the subjects' head by a specifically developed dual band antenna with transmit bands in the GSM900 and TETRA frequency range. The mechanical design of the developed antenna followed a concept previously described (Bahr et al., 2006; G Schmid et al., 2012), i.e. the antenna consisted of a planar, rectangular (120 mm × 45 mm) printed circuit board (PCB, made from 1.5 mm thick RO4003® substrate) with a 70 mm × 27 mm cutout to fit over the subject's ear (Fig. 2). As radiating element of the antenna, a so-called C-patch structure tuned to resonate at 385 MHz and 900 MHz was created by standard etching techniques from the (originally copper coated) RO4003® substrate in the upper quarter of the PCB, such that a RF absorption pattern in the temporal region of the head similar to the use of GSM900 or TETRA handsets was achieved when the antenna is attached to the subjects' head (Figure A1).

For GSM900, a carrier frequency signal of 915 MHz was modulated at approximately 217Hz with a duty cycle of 0.125. For TETRA, a 385 MHz carrier frequency was modulated at approximately 17.6 Hz

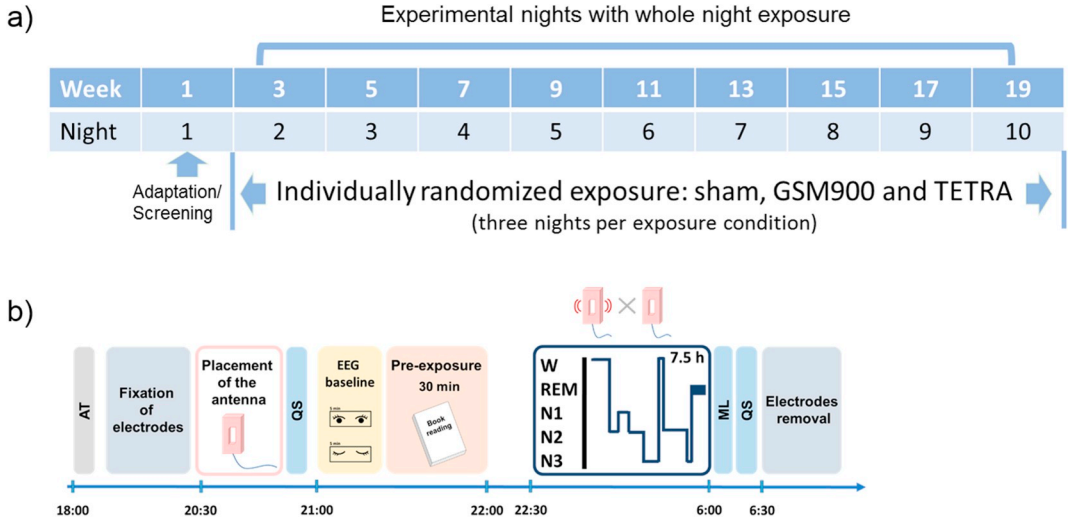


Fig. 1. Schematic overview of the study design (a) and of the nightly schedule in the sleep laboratory (b). The first night served as an adaptation and screening night. During the following nine study nights GSM900, TETRA and sham exposure were applied for three nights each in a rand omized, double-blind design. Participants arrived at the laboratory at 18:00 h and underwent an alcohol test (AT). If the results were negative (0.00 mg/l alcohol), electrodes were fixed. Immediately after the antenna was attached to the left ear, participants were allowed to read a book during a 30 min pre-exposure period (exception: during the first night, before reading, an EEG baseline recording was additionally performed with eyes closed and eyes open for 5 min each to check the inclusion criterion for the presence of an alpha EEG). Participants went to bed around 22:30 h. After exactly 7.5 h of sleep participants were awakened and they filled out a morning protocol (MP). Finally, electrodes were removed and participants were allowed to have breakfast and leave the lab.



Fig. 2. Side view of a subject's head immediately before going to bed. EEG, EOG and EMG electrodes were positioned for the upcoming PSG. Simultaneous to sleep recording, exposure was delivered by specifically designed antennas attached to the left ear (example of an antenna used in healthy elderly women).

with a duty cycle of 0.25.

Application of exposure approximated real life scenarios that are present during use of GSM900 mobile phone or TETRA radio handsets in contact with the head and ear under conditions where the radio transmitters of the handsets are set to maximum power. Based on computer simulations using high-resolution male and female anatomical head models and phantom measurements, the systems were adjusted to cause a peak spatial 10g average specific absorption rate (psSAR10g) of 6 W/kg for TETRA and 2 W/kg for GSM900, respectively, averaged over time in head tissues. These values are set to closely approach but not to exceed internationally accepted RF-EMF exposure limits recommended by ICNIRP (International Commission on Non Ionizing Radiation Protection) (ICNIRP, 1998, 2009) that have been incorporated into German legislation [2.0 W/kg for the general population; 10.0 W/kg for occupationally exposed subjects]. Hardware components of the exposure system were computer controlled by a specific control and monitoring software enabling double blinded and randomized application of the different exposure conditions specified in the study design. Resulting exposure of participants was automatically and continuously monitored (hidden from the study team and participant) by measuring forward and reflected power at the antenna input every 15 s and logging of these measurement data in encoded form on the computer, in order to ensure test subjects' safety and quality control of exposure data..

A brain region specific absorption analysis, taking into account uncertainties due to unavoidable variations of antenna position and anatomical variations of subjects' head revealed mass averaged SAR values of the temporal lobe in the ranges of 0.3–0.7 W/kg and 0.7–1.6 W/kg for GSM900 and TETRA exposure, respectively.

Moreover, the local temperature increase inside tissues next to the antenna caused by the RF exposure was analysed by computer simulations using anatomical head models. It is noted that this temperature increase is caused by three different mechanisms: (1) restriction of free air convection on the skin surface by the presence of the antenna (independent of exposure), (2) indirect heating from the antenna due to losses inside the antenna itself, and (3) due to RF absorption inside the tissue. The computer simulations indicated an overall tissue temperature increase in the skin of up to approx. 1.1 °C for the TETRA exposure at a psSAR10g of 6 W/kg and up to approx. 0.6 °C for the GSM900 exposure at a psSAR10g of 2 W/kg. These results are in line with earlier experimental investigations (Dorn et al., 2014), which in addition showed that the contribution of restriction of free air convection to the overall temperature increase may reach up to 0.25 °C. Exposure-related temperature increase in cortical brain regions was less than 0.2 °C and less than 0.1 °C for TETRA and GSM900 exposure, respectively.

2.5. Polysomnography

In both studies PSG was performed and recordings were evaluated according to the standard of the American Academy of Sleep Medicine (Iber et al., 2007). The six electrodes of this standard (F3, F4, C3, C4, O1, O2) to monitor the electrical activity of the brain were complemented by 13 further electrodes (Fp1, Fp2, Fz, F7, F8, Cz, T3, T4, Pz, P3, P4, T5, T6) to cover all 19 electrodes of the international 10–20 system (Jasper, 1958). An internal signal generated from C3 and C4 was used as physical reference for the recordings. For sleep scoring, contralateral mastoid electrodes M1 and M2 were used as references. Electrooculogram (EOG) signals were recorded using four electrode locations (left, right, upper, lower). These include the left and right EOG positions according to the standard of the American Academy of Sleep Medicine (Iber et al., 2007). A submental electromyogram (EMG) was recorded as a bipolar signal. Impedance of head electrodes was kept below 5 kOhm. Sampling rate for all signals was 200 Hz. A 70 Hz low pass filter was used. PSGs were recorded with a Nihon Kohden EEG2100 system. PSG recordings took place in a room in which the temperature was kept constant by air condition at an individually preferred level.

The headbox containing all analogue electronics was integrated into a shielding case of cast aluminium, including optical interfaces and RF suppressing filters. All input biosignals were led through two shielding chambers with inductor capacitor (LC) low pass filters of 5th order total.

It is necessary to keep RF signals away from the recorder electronics because they may cause artifacts in the circuitry and can lead to false positive results in studies on biological RF-EMF effects. Such artifacts could also compromise the blindness. Signals from and to the shielding box were led through optical cables or additional filters for the same reason. Effectiveness of these measures taken was checked by "PSG" recordings of a water melon that served as a dummy for the human head under sham and verum exposures. Electrode and antenna placement were carried out very similar to the PSG recordings on subjects. Another type of interference between RF-EMF exposure and simultaneous EEG recordings results from the electrode cables. Due to their conductive properties they may reduce tangential field strengths on the subject's head and can induce additional RF currents under some locations. Both effects are reduced by adding distributed RF impedance to the electrode cables. In the studies described here, a thin stainless steel spring material, insulated and protected by polyolefine shrink tubing was used to produce special electrode cables. The construction implies inductive and also some resistive impedance and reduces the changes of the RF field distribution compared to conventional EEG cables. This was confirmed by phantom measurements.

To reduce inter-rater variability of results, the PSGs were scored using a computer assisted algorithm (Somnolyzer 24 × 7) according to the standard of the American Academy of Sleep Medicine (Iber et al.,

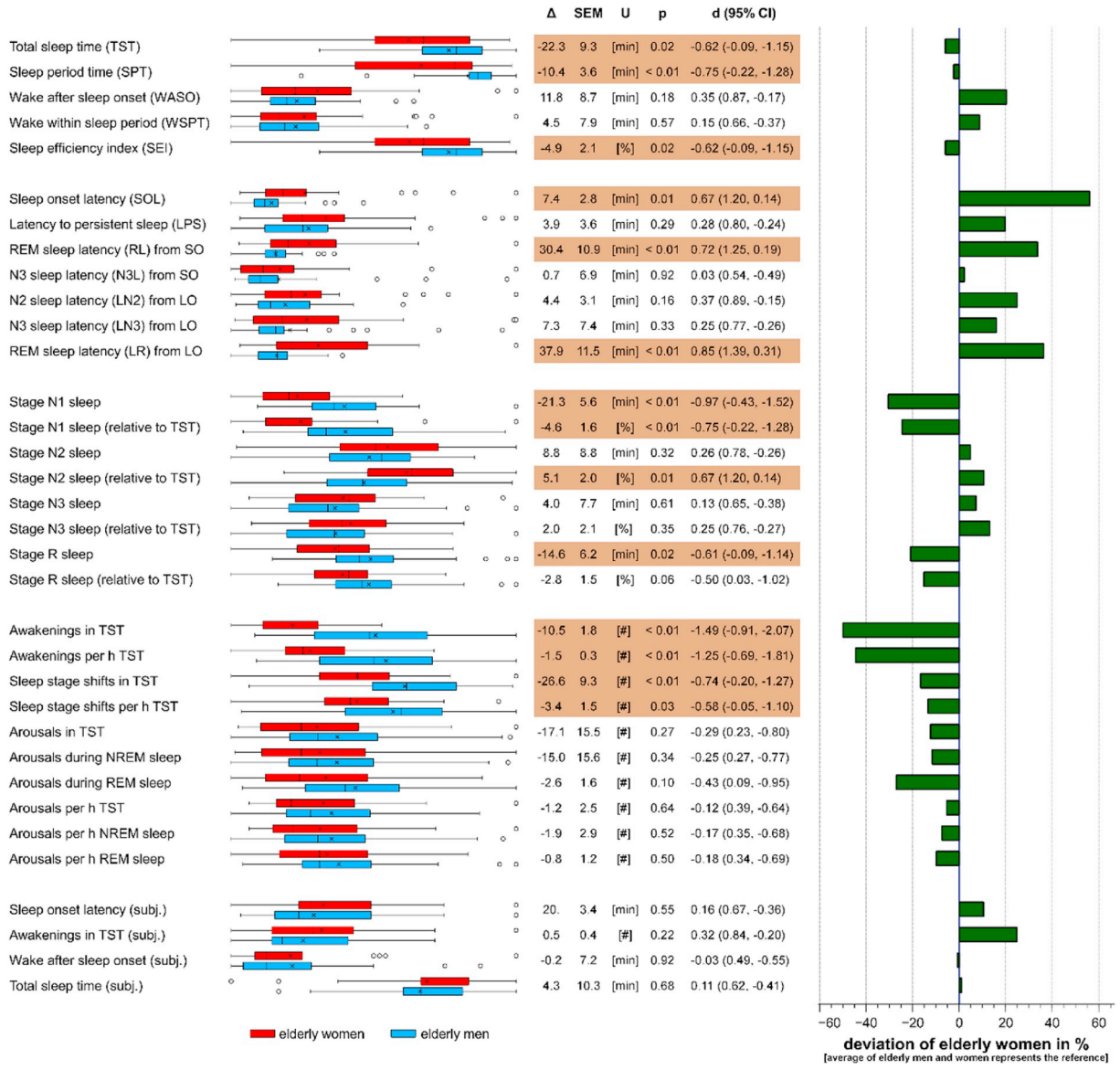


Fig. 3. Sex differences in sleep parameters observed under sham exposure. The figure shows the sham value distributions of all sleep parameters under investigation for elderly men and women as boxplots. Please note that a representation of the individual x-axes has been omitted in order not to overload the figure. The differences refer to the following Δ: women minus men. The right part of the figure illustrates the differences in relation to the average values of elderly women and men expressed as percentages. SEM = standard error; U = unit; p = significance level; d = Effect size estimate Cohen's d for an independent group comparison. The 95% CI (confidence interval) is given in brackets.

2007) including a final check of the results by a human expert. This scoring procedure is FDA (Food and Drug Administration) approved (Anderer et al., 2010).

The recording time (or time in bed; TIB in min) was kept constant at 450 min. Altogether, 24 parameters describing the macrostructure of sleep were considered: TST in min, sleep period time (SPT in min), WASO in min, wake within SPT (WSPT in min), sleep efficiency index (SEI in %), SOL in min, latency to persistent sleep (LPS in min), latencies from "lights out to stages" R, N2, N3 (LR, LN2, LN3 in min), latencies from sleep onset to stages R and N3 (RL, N3L in min) time in each sleep stage (N1, N2, N2, R in min), percent of TST in each sleep stage (N1, N2, N3, R in %), awakenings and stage shifts (absolute numbers and numbers per hour TST, respectively). Furthermore, six variables characterizing arousals from sleep (during TST, NREM sleep and REM sleep; expressed in numbers and as indices, i.e. per h of the respective sleep stage) were considered (Table A3).

2.6. Subjective sleep quality

While PSG provides information on objective aspects of sleep, subjective information on SOL, number of awakenings, WASO and TST were collected (Table A3) by means of standardised morning protocols (Hoffmann et al., 1997).

2.7. Statistics

In both studies, data analysis followed the same conservative approach. Prior to application of statistical tests data of the same exposure condition were pooled at the individual level by computing robust means (median) for each of the 30 objective and four subjective outcome variables. This procedure reduced random variance.

In a first step, a limited data set comprising only those values recorded under sham exposure was statistically analysed using independent two-sample t-tests to identify possible physiological differences in outcome parameters irrespective of exposure. If the assumption

Table 3
Results of the mixed design ANOVAs with GSM900 and sham as levels of EXPOSURE for 30 objective and four subjective sleep parameters. Statistically significant results are highlighted in grey and marked in bold. Degrees of freedom numbers are in parentheses behind the factor labels.

		Sex (†:1, 58; ‡: 1, 56)				Exposure (†:1, 58; ‡: 1, 56)				Sex * exposure (†:1, 58; ‡: 1, 56)			
Parameter	Unit	F	p	η_p^2	η_G^2	F	p	η_p^2	η_G^2	F	p	η_p^2	η_G^2
Total sleep time (TST) †	min	4.86	**0.03**	0.077	0.065	0.25	0.62	0.004	0.001	0.77	0.38	0.013	0.002
Sleep period time (SPT) †	min	9.62	< **0.01**	0.142	0.119	3.65	0.06	0.059	0.010	0.49	0.49	0.008	0.001
Wake after sleep onset (WASO) †	min	1.12	0.29	0.019	0.014	0.42	0.52	0.007	0.002	1.12	0.29	0.019	0.005
Wake within sleep period (WSPT) †	min	0.05	0.83	0.001	0.001	0.68	0.41	0.012	0.003	0.61	0.44	0.010	0.003
Sleep efficiency index (SEI) †	%	4.74	**0.03**	0.076	0.063	0.28	0.60	0.005	0.001	0.84	0.36	0.014	0.002
Sleep onset latency (SOL) †	min	5.85	**0.02**	0.092	0.084	2.34	0.13	0.039	0.003	0.95	0.33	0.016	0.001
Latency to persistent sleep (LPS) †	min	0.68	0.41	0.012	0.009	3.30	0.07	0.054	0.011	0.50	0.48	0.009	0.002
REM sleep latency (RL) from SO †	min	5.78	**0.02**	0.091	0.072	1.21	0.28	0.020	0.004	5.49	**0.02**	0.086	0.018
N3 sleep latency (N3L) from SO †	min	0.07	0.79	0.001	0.001	3.59	0.06	0.058	0.014	0.58	0.45	0.010	0.002
N2 sleep latency (LN2) from LO †	min	1.14	0.29	0.019	0.017	1.33	0.25	0.022	0.002	1.57	0.21	0.026	0.003
N3 sleep latency (LN3) from LO †	min	0.84	0.36	0.014	0.011	5.05	**0.03**	0.080	0.018	0.53	0.47	0.009	0.002
REM sleep latency (LR) from LO †	min	9.06	< **0.01**	0.135	0.104	2.18	0.15	0.036	0.008	5.68	**0.02**	0.089	0.020
Stage N1 sleep †	min	25.37	< **0.01**	0.304	0.258	3.00	0.09	0.049	0.008	0.63	0.43	0.011	0.002
Stage N1 sleep of TST †	%	19.37	< **0.01**	0.250	0.204	3.84	0.05	0.062	0.012	1.74	0.19	0.029	0.005
Stage N2 sleep †	min	2.70	0.11	0.044	0.039	1.64	0.20	0.027	0.003	2.96	0.09	0.049	0.006
Stage N2 sleep of TST †	%	8.33	< **0.01**	0.126	0.114	1.59	0.21	0.027	0.002	0.45	0.51	0.008	0.001
Stage N3 sleep †	min	0.96	0.33	0.016	0.015	0.32	0.57	0.005	0.000	2.71	0.11	0.045	0.003
Stage N3 sleep of TST †	%	1.58	0.21	0.027	0.025	1.55	0.22	0.026	0.002	0.97	0.33	0.016	0.001
Stage REM sleep †	min	5.18	**0.03**	0.082	0.067	0.08	0.78	0.001	0.000	0.66	0.42	0.011	0.002
Stage REM sleep of TST †	%	3.45	0.07	0.056	0.047	0.02	0.88	0.000	0.000	0.27	0.60	0.005	0.001
Awakenings in TST †	#	34.81	< **0.01**	0.375	0.346	0.18	0.67	0.003	0.000	0.05	0.82	0.001	0.000
Awakenings/h TST †	#	26.12	< **0.01**	0.311	0.281	0.96	0.33	0.016	0.002	0.09	0.77	0.002	0.000
Sleep stage shifts in TST †	#	11.95	< **0.01**	0.171	0.147	2.28	0.14	0.038	0.005	0.84	0.36	0.014	0.002
Sleep stage shifts/h TST †	#	7.40	< **0.01**	0.113	0.098	2.20	0.14	0.037	0.005	0.74	0.39	0.013	0.002
Arousals in TST †	#	2.36	0.13	0.039	0.035	3.28	0.08	0.054	0.006	0.78	0.38	0.013	0.001
Arousals during NREM sleep †	#	1.61	0.21	0.027	0.024	3.51	0.07	0.057	0.006	0.39	0.54	0.007	0.001
Arousals during REM sleep †	#	7.27	< **0.01**	0.111	0.089	2.52	0.12	0.042	0.009	2.10	0.15	0.035	0.007
Arousals/h TST †	#	1.10	0.30	0.019	0.016	4.55	**0.04**	0.073	0.010	1.91	0.17	0.032	0.004
Arousals/h NREM sleep †	#	1.28	0.26	0.022	0.019	4.77	**0.03**	0.076	0.009	1.38	0.24	0.023	0.003
Arousals/h REM sleep †	#	2.38	0.13	0.039	0.034	7.46	< **0.01**	0.114	0.016	3.64	0.06	0.059	0.008
Sleep onset latency † (subjective)	min	0.08	0.77	0.001	0.001	0.48	0.49	0.008	0.002	3.15	0.08	0.051	0.010
Awakenings in TST ‡ (subjective)	#	0.10	0.75	0.002	0.001	1.84	0.18	0.032	0.007	6.16	**0.02**	0.099	0.024
Wake after sleep onset ‡ (subjective)	min	0.15	0.70	0.003	0.002	1.64	0.21	0.028	0.006	0.49	0.49	0.009	0.002
Total sleep time † (subjective)	min	2.16	0.15	0.036	0.029	0.46	0.50	0.008	0.002	4.39	**0.04**	0.070	0.015

F = F-statistic; p = significance level; η_p^2 = partial eta squared; η_G^2 = generalized eta squared [According to Lakens (2013) only η_G^2 can be compared to the following benchmarks provided by Cohen (1988): $\eta_G^2 < 0.010$ representing no effect, $0.010 \leq \eta_G^2 < 0.060$ representing a small effect, $0.060 \leq \eta_G^2 < 0.140$ representing a medium effect and $\eta_G^2 \geq 0.140$ representing a large effect].

of homogeneity of variances was violated, the Satterthwaite approximation was used to estimate the effective degrees of freedom. Then, to explore possible RF-EMF effects outcome variables were statistically analysed using mixed design analyses of variances (ANOVAs) with SEX as between-subject factor, EXPOSURE as within-subject factor and the INTERACTION between these two main factors. As it was not intended to account for all three exposure conditions within the same statistical model, separate mixed design ANOVAs with either GSM and sham or TETRA and sham as levels of EXPOSURE, respectively, were performed. Finally, within sample pairwise analyses (t-tests for paired observations) based on individual differences between the verum and sham exposure conditions were performed to investigate sex-specific RF-EMF effects on sleep macrostructure.

In order to facilitate the interpretation of observed effects, enable comparisons of effects across studies, and allow for a-priori power analyses, estimates of effect sizes are useful (Lakens, 2013). For the mixed design ANOVAs paritial eta squared (η_p^2) and generalized eta squared (η_G^2 (Olejnik and Algina, 2003);) values are reported. According to Lakens (2013), the former can be used for sample size calculations and to compare effects between studies with similar designs, while the latter can be interpreted against suggested benchmarks ($\eta_G^2 < 0.010$: no effect; $0.010 \leq \eta_G^2 < 0.060$: small effect, $0.060 \leq \eta_G^2 < 0.140$: medium effect and $\eta_G^2 \geq 0.140$: large effect) and allows for comparison of effects between studies with different experimental designs. For the univariate tests, either Cohen's d for independent group comparisons or Cohen's d_{av} for paired sample comparions was reported as measure of effect size. A SAS macro written by Kadel and Kip (2012) was used for computing the corresponding 95% confidence intervals (CI). According to Cohen's conventions (Cohen, 1988) $d < 0.2$ represents no effect, $0.2 \leq d < 0.5$ represents a small effect, $0.5 \leq d < 0.8$ represents a medium effect and $d \geq 0.8$ represents a large effect.

All statistical analyses, tested with a double-sided alpha of 0.05, were conducted with SAS (version 9.4).

3. Results

Participant flow diagrams for the studies in elderly women and men are shown in Figures A2 and A.3, respectively. A comparison of the two final samples considered for statistical analyses with regard to age revealed that males were slightly, but not statistically significant older than females (mean ± standard deviation: 69.1 ± 5.5 years vs 67.8 ± 5.7 years; p = 0.39).

3.1. Physiological differences in objective and subjective sleep parameters between elderly men and women

Data presented in Fig. 3 indicate that sleep recorded under sham exposure differed significantly between elderly men and women in 47% of the considered objective sleep variables (14 out of 30) while at the subjective level the four sleep variables did not differ (for descriptive statistics see Tables A4 and A5 in the Appendix). Elderly women have a significantly shorter TST and SPT, as well as a lower sleep efficiency index. They need longer to fall asleep (only to the first occurrence of any sleep stage, they do, however, not need significantly longer to reach

10 min of persistent sleep). These differences at a first glance indicate that sleep of elderly women is worse than that of elderly men. However, once sleep started, the quality of sleep is better in elderly women than in elderly men as documented by significantly less light sleep (stage N1 in min and % of TST), and less sleep stage changes and awakenings (both in absolute numbers and as index, i.e. per hour of sleep). Furthermore, women have significantly more stage N2 sleep (as % of TST), they reach stage R significantly later as compared to men (from both lights out and sleep onset), and the amount of stage R sleep (min) is significantly less.

3.2. Effects of GSM900 exposure ($psSAR_{10g}$ = 2.0 W/kg) on objective and subjective sleep parameters in elderly men and women

The mixed design ANOVAs with GSM900 and sham as the two levels of EXPOSURE show that SEX affects 50% of the objective and none of the subjective parameters significantly (Table 3). Fourteen out of the 15 affected objective parameters show also sex differences under sham exposure. The pattern of sex effects on these variables was the same as observed under sham (see Fig. 3 as well as Tables A4 and A5 in the Appendix). Additionally, arousals during stage R sleep do show a significant SEX effect in the multivariate statistical model. The number of arousals during stage R sleep is lower in women as compared to men (Tables A4 and A5). This difference does, however, not reach statistical significance in the sham condition (p = 0.10; Fig. 3).

Significant EXPOSURE effects are observed for the arousal indices during TST, NREM sleep and REM sleep, as well as for the latency from lights out to the first occurrence of stage N3 sleep (Table 3). The arousal indices are lower under GSM900 exposure as compared to sham, while the stage N3 sleep occurs earlier when subjects are GSM900-exposed (Tables A4 and A5). Finally, the results displayed in Table 3 indicate that both latencies to the occurrence of stage R sleep (from sleep onset and from lights out) as well as the perceived number of awakenings and the TST are differentialy affected by EXPOSURE in men and women. In women the latencies and the number of awakenings tend to decrease with exposure, while in men they tend to increase or do not differ. On the contrary, subjectively rated TST tend to be longer in women and shorter in men under exposure (Tables A4 and A5). However, a post-hoc univariate sex-specific analysis of GSM900 exposure effects revealed that of these four variables, only the differences in the distributions of the latency to stage R sleep from lights out and the perceived number of awakenings observed in women are statistically significant (Figure A4). Univariate analysis provided further statistically significant results, but again only for women. GSM900 compared to sham led to shorter latencies to the occurrence of stage N3 sleep (from sleep onset and from lights out), decreased the amount of stage N1 sleep (in min and % of TST) and reduced the number of arousals during REM sleep (both in absolute numbers and as index; Figure A4).

3.3. Effects of TETRA exposure ($psSAR_{10g}$ = 6.0 W/kg) on objective and subjective sleep parameters in elderly men and women

The statistical model with TETRA and sham as the two levels of EXPOSURE shows that SEX affects 40% of the objective and none of the subjective sleep parameters significantly (Table 4). There is again a large overlap with those variables that were already significantly different between men and women in the sham condition (see Fig. 3 as well as Tables A4 and A5): the SPT, SOL, stage R sleep latency (from lights out), stage N1 (both in min and as % of TST), stage N2 sleep (% of TST), stage R sleep (min), as well as the number and index per hour of sleep of awakenings and stage shifts. Additionally, stage R sleep (% of TST) is significantly affected by SEX in the multivariate model. In line with the amount of stage R sleep in minutes the percentage of stage R sleep is lower in women as compared to men (Tables A4 and A5). In the sham condition this difference failed to reach statistical significance (p = 0.06; Fig. 3).

Two objective and one subjective sleep parameter(s) are significantly affected by EXPOSURE: the number and index of arousal during stage R sleep as well as the subjectively estimated duration of wake after sleep onset (WASO; Table 4). There are less arousals from stage R sleep (both in absolute numbers and as index expressed per hour of sleep) and subjects felt that they were less awake after sleep onset in the TETRA condition as compared to sham (Tables A4 and A5). Finally, the results displayed in Table 4 indicate that wake within the sleep period time, stage N3 latency (from sleep onset) and stage R latency (both from lights out and from sleep onset) are affected differently by TETRA in men and women. In women the latencies and wake within the sleep period time tend to be shorter, while in men latencies and wake tend to be longer or do not differ (Tables A4 and A5). In women, all of these four differences were also statistically significant at the univariate level as revealed by post-hoc gender-specific analyses of TETRA effects (Figure A5). Additionally, TETRA reduced the number of arousals during stage R sleep (both in absolute numbers and as index expressed per hour of sleep) and led to a shorter perceived wake time after sleep onset. In men, however, only the absolute number of arousals during stage R sleep was significantly less under TETRA (Figure A5).

4. Discussion

Of the 20 studies that dealt with the macrostructure of sleep, the majority (n = 12) examined subjects up to the age of 30 (Borbely et al., 1999; Danker-Hopfe et al., 2011; Danker-Hopfe et al., 2016; Hinrichs et al., 2005; Huber et al., 2000; Huber et al., 2002; Hung et al., 2007; Lustenberger et al., 2013; Lustenberger et al., 2015; Regel et al., 2007; MR Schmid et al., 2012a; MR Schmid et al., 2012b). Except for one study, only male subjects were investigated. Hinrichs et al. (2005) were the only ones who considered young females (12 out of 13 subjects). Four out of five studies considered male subjects up to the age of 39 (Fritzer et al., 2007; Mann and Roschke, 1996; Wagner et al. 1998, 2000). Nakatani-Enomoto et al. (2013) investigated 7 females and 12 males up to the age of 39 years. Only three studies covered a broader age range and both sexes (Loughran et al., 2005: 18–60 years, 23 females and 27 males; Loughran et al., 2012: 20–51 years, 13 females and 7 males; Lowden et al., 2011: 18–44 years, 27 females and 21 males). In contrast, subjects older than 60 years as well as gender differences were not investigated in any of the studies conducted to date. Nakatani-Enomoto et al. (2013), however, speculate that sleep of elderly subjects might be impaired by exposure to RF-EMF.

The present results indicate that there are pronounced differences in objectively assessed sleep parameters between men and women. However, 20% of the parameters are also affected by either GSM900 or TETRA directly or by interaction.

Specifically, arousal parameters but also stage N3 latency (exposure to GSM900 only) are affected (significant exposure effects) in men and women in the same way. They show less arousal under GSM900 and TETRA, respectively, as compared to sham, and a shorter latency to stage N3 sleep. The observed changes, however, do not reflect a disturbance of sleep, e.g. a negative health effect. They can rather be interpreted as changes towards a more consolidated and hence better sleep. This is also confirmed by the results of TETRA effects on subjective sleep parameters. TETRA leads to a reduction of the perceived time subjects spent awake after sleep onset in men as well as in women.

Other parameters are affected differently in men and women as indicated by significant interaction terms. GSM900 and TETRA exposure lead to a reduction of the time needed from lights out and sleep onset, respectively, to reach stage R sleep in women, but not in men. Furthermore, TETRA leads to a reduction of the time spent awake within the sleep period time and the time needed from sleep onset to reach stage N3 sleep in women, but not in men. At a subjective level the number of awakenings was lower under GSM900 im women, but not in men and the TST was longer in women but not in men.

Table 4
Results of the mixed design ANOVAs with TETRA and sham as levels of EXPOSURE for 30 objective and four subjective sleep parameters. Statistically significant results are highlighted in grey and marked in bold. Degrees of freedom numbers are in parentheses behind the factor labels.

		Sex (†:1, 58; ‡: 1, 56)				Exposure (†:1, 58; ‡: 1, 56)				Sex * exposure (†:1, 58; ‡: 1, 56)			
Parameter	Unit	F	p	η_p^2	η_G^2	F	p	η_p^2	η_G^2	F	p	η_p^2	η_G^2
Total sleep time (TST) †	min	2.86	0.10	0.047	0.040	0.57	0.45	0.010	0.001	3.93	0.05	0.063	0.010
Sleep period time (SPT) †	min	10.96	< **0.01**	0.159	0.123	0.00	0.99	0.000	0.000	0.30	0.59	0.005	0.001
Wake after sleep onset (WASO) †	min	0.70	0.40	0.012	0.010	0.24	0.62	0.004	0.001	2.41	0.13	0.040	0.008
Wake within sleep period (WSPT) †	min	0.41	0.53	0.007	0.005	2.04	0.16	0.034	0.008	5.88	**0.02**	0.092	0.023
Sleep efficiency index (SEI) †	%	2.87	0.10	0.047	0.040	0.59	0.45	0.010	0.001	3.83	0.06	0.062	0.010
Sleep onset latency (SOL) †	min	8.54	< **0.01**	0.128	0.097	1.24	0.27	0.021	0.005	0.60	0.44	0.010	0.003
Latency to persistent sleep (LPS) †	min	2.32	0.13	0.038	0.027	0.25	0.62	0.004	0.001	0.24	0.63	0.004	0.001
REM sleep latency (RL) from SO †	min	3.60	0.06	0.058	0.047	2.47	0.12	0.041	0.007	8.70	< **0.01**	0.130	0.025
N3 sleep latency (N3L) from SO †	min	0.92	0.34	0.016	0.012	3.22	0.08	0.053	0.011	4.38	**0.04**	0.070	0.016
N2 sleep latency (LN2) from LO †	min	1.70	0.20	0.028	0.021	0.30	0.59	0.005	0.001	0.57	0.45	0.010	0.002
N3 sleep latency (LN3) from LO †	min	0.20	0.66	0.003	0.003	1.83	0.18	0.031	0.006	2.39	0.13	0.040	0.008
REM sleep latency (LR) from LO †	min	5.62	**0.02**	0.088	0.076	3.33	0.07	0.054	0.007	8.75	< **0.01**	0.131	0.018
Stage N1 sleep †	min	19.17	< **0.01**	0.248	0.220	0.58	0.45	0.010	0.001	0.15	0.70	0.003	0.000
Stage N1 sleep of TST †	%	14.52	< **0.01**	0.200	0.169	0.69	0.41	0.012	0.002	0.94	0.34	0.016	0.002
Stage N2 sleep †	min	1.66	0.20	0.028	0.024	0.10	0.75	0.002	0.000	0.46	0.50	0.008	0.001
Stage N2 sleep of TST †	%	8.27	< **0.01**	0.125	0.112	0.08	0.79	0.001	0.000	0.13	0.72	0.002	0.000
Stage N3 sleep †	min	0.66	0.42	0.011	0.010	2.20	0.14	0.037	0.002	1.34	0.25	0.023	0.002
Stage N3 sleep of TST †	%	1.30	0.26	0.022	0.020	1.02	0.32	0.017	0.001	0.52	0.48	0.009	0.001
Stage REM sleep †	min	6.70	**0.01**	0.104	0.090	0.34	0.56	0.006	0.001	0.00	0.98	0.000	0.000
Stage REM sleep of TST †	%	5.35	**0.02**	0.084	0.074	0.86	0.36	0.015	0.002	0.23	0.63	0.004	0.000
Awakenings in TST †	#	38.47	< **0.01**	0.399	0.375	0.20	0.66	0.003	0.000	0.15	0.70	0.003	0.000
Awakenings/h TST †	#	29.34	< **0.01**	0.336	0.312	0.00	0.96	0.000	0.000	0.68	0.41	0.012	0.001
Sleep stage shifts in TST †	#	10.81	< **0.01**	0.157	0.137	0.00	0.97	0.000	0.000	0.37	0.55	0.006	0.001
Sleep stage shifts/h TST †	#	6.84	**0.01**	0.105	0.093	0.00	0.98	0.000	0.000	0.50	0.48	0.009	0.001
Arousals in TST †	#	1.58	0.21	0.027	0.025	1.00	0.32	0.017	0.001	0.09	0.77	0.002	0.000
Arousals during NREM sleep †	#	1.24	0.27	0.021	0.019	0.39	0.53	0.007	0.000	0.12	0.73	0.002	0.000
Arousals during REM sleep †	#	3.52	0.07	0.057	0.048	9.58	< **0.01**	0.142	0.026	0.00	0.96	0.000	0.000
Arousals/h TST †	#	0.84	0.36	0.014	0.013	1.06	0.31	0.018	0.002	2.04	0.16	0.034	0.003
Arousals/h NREM sleep †	#	1.19	0.28	0.020	0.018	0.87	0.36	0.015	0.001	1.79	0.19	0.030	0.003
Arousals/h REM sleep †	#	1.02	0.32	0.017	0.014	9.34	< **0.01**	0.139	0.027	0.17	0.68	0.003	0.001
Sleep onset latency † (subjective)	min	0.10	0.76	0.002	0.001	0.17	0.68	0.003	0.001	3.85	0.05	0.062	0.012
Awakenings in TST ‡ (subjective)	#	0.93	0.34	0.016	0.015	0.02	0.89	0.000	0.000	1.78	0.19	0.031	0.003
Wake after sleep onset ‡ (subjective)	min	0.17	0.68	0.003	0.003	6.72	**0.01**	0.107	0.019	0.73	0.40	0.013	0.002
Total sleep time † (subjective)	min	0.99	0.32	0.017	0.013	0.00	0.98	0.000	0.000	1.00	0.32	0.017	0.004

F = F-statistic; p = significance level; η_p^2 = partial eta squared; η_G^2 = generalized eta squared [According to Lakens (2013) only η_G^2 can be compared to the following benchmarks provided by Cohen (1988): $\eta_G^2 < 0.010$ representing no effect, $0.010 \leq \eta_G^2 < 0.060$ representing a small effect, $0.060 \leq \eta_G^2 < 0.140$ representing a medium effect and $\eta_G^2 \geq 0.140$ representing a large effect].

Overall, the data indicate, that the sleep of elderly women is more affected by RF-EMF exposure than sleep of elderly men. None of the observed changes, however, indicates sleep disturbing effects of RF-EMF exposure. A strength of the present results is that statistical analyses are based on robust estimates of sleep parameters under different exposure conditions (individual means for three nights under each exposure condition) which reduced the probability of random effects.

Analysis of sleep in previous studies yielded heterogeneous and partly contradicting results (see Table 1). The comparability of study results is limited by various factors. The number of sleep variables, which were considered or reported varied by study from 1 (Borbely et al., 1999) to 177 (Danker-Hopfe et al., 2011). The majority of studies (16 of 20) considered less than 15 variables. Most analyses refer to parameters reported for the whole night. There are few studies, which also looked at results by sleep cycle or quarters/thirds of the night. When subjects are exposed exclusively prior to sleep for 30 min (Huber et al., 2000; Huber et al., 2002; Hung et al., 2007; Loughran et al., 2005; Loughran et al., 2012; Lustenberger et al., 2015; Regel et al., 2007; MR Schmid et al., 2012a; MR Schmid et al., 2012b) or for 3 h (Lowden et al., 2011; Nakatani-Enomoto et al., 2013), effects might be expected to occur early in the night. Thus, an analysis of the macrostructure of sleep for the whole night might limit the conclusion from these studies. Earlier results, which also point towards a better sleep under exposure, are a reduced SOL observed by Mann & Röschke (1996), a reduced WASO observed by Borbély et al. (1999), and a reduced number of stage shifts towards lighter sleep (stage N1) observed by Danker-Hopfe et al. (2011). All of these observations were made in samples of young healthy men.

The reduction of arousals from sleep observed for elderly men and women under both exposure conditions was not reported in previous studies. This, however, could be due to the fact that only few studies looked specifically at arousal parameters and those who did (Hinrichs et al., 2005: 20–28 year old men (n = 1) and women (n = 12); Loughran et al., 2012: 20–51 year old men (n = 7) and women (n = 13); Lowden et al., 2011: 18–44 year old men (n = 21) and women (n = 27); Nakatani-Enomoto et al., 2013: 22–39 year old men (n = 12) and women (n = 7)), did not differentiate between arousals during NREM sleep and REM sleep.

Back in 1996 Pasche et al. (1996) administered RF-EMF delivered by a mouth piece located between tongue and palate (three times a week, total 12 applications) for 20 min in the afternoon for treatment of insomnia. They investigated the effectiveness of this low energy emission therapy in 106 subjects (59 women and 47 men in the age range between 21 and 55 years) with psychophysiological insomnia. In a parallel-group design subjects were randomized to either active or inactive exposure. In that study, they found an increment in TST and a reduction in SOL, which were their primary outcome parameters. TST increased significantly by 76.0 ± 11.1 min from baseline to post treatment. This change was significantly larger than the corresponding change in the inactive group (20.0 ± 13.5 min). However, at baseline the TST was significantly lower in the active group as compared to the inactive group. TST post treatment did not differ significantly between groups. Similarly, SOL decreased by 21.6 ± 5.9 min in the active group and by 6.0 ± 6.0 min in the inactive group. They started with

similar sleep latencies at baseline. Deviating from the other studies discussed here, EMF was not delivered by an antenna, but a direct electrical contact of a mouth piece with the mucosa.

Benefical effects of RF-EMF exposure on sleep have also been reported in vivo studies performed with young Wistar rats (Pelletier et al. 2013, 2014). Juvenile Wistar rats (n = 13) which were exposed for 5 weeks at 24 °C air temperature to RF-EMF (900 MHz, 1 V/m). Exposed rats had 14.6% more slow wave sleep, while paradoxical sleep (REM sleep) was not affected in this study (Pelletier et al., 2014). The authors conclude that the observed changes in sleep under exposure may involve signals from thermoreceptors in the skin.

This argumentation is in a line with results from a human study. Danker-Hopfe et al. (2016), who reported more stage R sleep under GSM and Wideband Code Division Multiple Access (WCDMA) exposure as compared to sham exposure in young healthy male subjects, argued that these might be mediated by thermal exposure of the skin. In the preoptic area (POA) of the hypothalamus neurons involved in sleep regulation (Saper et al. 2001, 2010) and thermoregulation (Romanovsky, 2018; Te Lindert and Van Someren, 2018; Van Someren, 2000) are in close neighborhood. According to Benarroch (2007) the warm sensitive (WS) neurons of the POA are also directly involved in sleep regulation. The close association between the circadian rhythm, sleep propensity and core body temperature is well documented (for a review see Te Lindert and Van Someren, 2018). These authors discuss in detail the associations between body core temperature and proximal as well as skin temperature. Based on observational and experimental human studies they argue that skin temperature can affect sleep and vigilance. Raymann and Van Someren (2008) demonstrated that a mild distal warming (0.4 °C, with almost no effect on core temperature) lead to changes in sleep in small samples of young and elderly subjects as well as in patients with insomnia. The warming specifically facilitated sleep onset in eight healthy elderly subjects (by 18%) and in eight elderly patients with insomnia (by 28%). Both samples comprised four men and four women.

Thermosensitivity of the body surface decreases with increasing age (Stevens and Choo, 1998). They showed that thermosensitivity varied approximately 100 fold across the 13 investigated regions of the body surface, with the face being most sensitive. With aging thermal sensitivity declines, this decline is more pronounced at the extremities than at central body regions. Romanovsky (2018) pointed out that although the surface area of the human face is comparatively small (approximately 4–5% of the total skin area), it accounts for a large share of the thermosignalling from the skin since due to the high density of thermoreceptors in the face. There are not only age related changes in thermosensitivity, but also sex differences. Inoue et al. (2016) who investigated thermal sensitivity in young and elderly men and women (mean ages ± standard error of the mean [years]: young women 21.6 ± 0.2; young men: 21.2 ± 0.4; elderly women: 65.2 ± 1.0; elderly men: 66.2 ± 1.5) that elderly had a lower thermal sensitivity at eight body locations than younger subjects. This was true for women and for men. Women in each age group had a lower thermal sensitivity than males. The forehead was consistently the most sensitive of all eight in young and in elderly as well as in women and in men.

The applied RF exposure causes an increase of skin temperature. For example, the TETRA exposure (max psSAR10g of 6 W/kg) used in the present study leads to an increase in skin temperature of up to 1.1 °C (see exposure systems and dosimetry). Previous research has shown that subjects are not able to perceive this RF-induced increase of skin temperature and thus this did not compromise blinding (Dorn et al., 2014).

Given the fact that a) our device to deliver RF-EMF exposure at the head leads to an increase in skin temperature, b) the face is an important region for thermosignalling to the brain, c) slight increases in skin temperature have an effect on sleep, and d) thermosensitivity is different between elderly men and women it may be speculated whether the observed sex differences in effects of RF-EMF exposure between men and women can be explained in terms of skin mediated thermoregulatory mechanisms. This hypothesis could be tested by conducting a sham-controlled study with a similar design to the present one in which an “antenna” is used which, without emitting radiofrequency electromagnetic fields, just heats the same part of the head as the real exposure.

If similar effects on sleep can be observed with just a localized heating of the skin region that was affected to elevated temperatures due to our experimental RF-EMF then research is indicated to explore whether warmth application in such a skin region can be used for treatment of insomnia, specifically in elderly females.

5. Conclusion

This is the first study, which not only includes but also specifically investigates elderly subjects and looks at possible gender differences in response to RF-EMF. In summary, the present results indicate that elderly women are more affected by RF-EMF exposure than elderly men. The observed changes are indicative of a sleep promoting effect of exposure. It is hypothesized that effects are mediated by skin related thermoregulatory mechanisms. A limitation is that these results cannot be generalized to men and women of all ages.

Ethics and financial disclosure

Both studies were approved by the ethics committee of the Charité – University Medicine, Berlin (EA4/122/13 for both studies) and are registered on ClinicalTrials.gov:

Study in elderly women

Registry name: Radiofrequency Electromagnetic Field (RF-EMF) Effects on Brain Activity During Sleep and Waking in Healthy Elderly Women (EMF60 + women)

URL: https://clinicaltrials.gov/ct2/show/NCT02906228?term = EMF&rank = 4

Registry number: NCT02906228

Study in elderly men

Registry name: RF-EMF Effects on the CNS in Elderly Men (EMF60 + males).

URL: https://clinicaltrials.gov/ct2/show/NCT02896491?term = EMF&rank = 1

Registry number: NCT02896491

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.109181.

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