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THEORETICAL REVIEW

The potential for impact of man-made super low and extremely low frequency electromagnetic fields on sleep

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S U M M A R Y

An ever-growing number of electromagnetic (EM) emission sources elicits health concerns, particularly stemming from the ubiquitous low to extremely low frequency fields from power lines and appliances, and the radiofrequency fields emitted from telecommunication devices. In this article we review the state of knowledge regarding possible impacts of electromagnetic fields on melatonin secretion and on sleep structure and the electroencephalogram of humans. Most of the studies on the effects of melatonin on humans have been conducted in the presence of EM fields, focusing on the effects of occupational or residential exposures. While some of the earlier studies indicated that EM fields may have a suppressive effect on melatonin, the results cannot be generalized because of the large variability in exposure conditions and other factors that may influence melatonin. For instance, exposure to radiofrequency EM fields on sleep architecture show little or no effect. However, a number of studies show that pulsating radiofrequency electromagnetic fields, such as those emitted from cellular phones, can alter brain physiology, increasing the electroencephalogram power in selective bands when administered immediately prior to or during sleep. Additional research is necessary that would include older populations and evaluate the interactions of EM fields in different frequency ranges to examine their effects on sleep in humans.

Introduction

While mass electrification is only about 100 y old, it is now nearly impossible to imagine living in a society without electrically powered devices. However, by operating any electrical device, an artificial electromagnetic (EM) radiation (a form of energy) is generated that overlays and modifies the universal time-varying electromagnetic fields (EMF) existing at the earth's surface. Fig. 1 reviews the broad groups of natural EM radiation on the Earth's surface environment; these range in frequency (equal energy) from cosmic gamma rays (10^{20} Hz) and x-rays (10^{18} Hz) down to microwaves (10^{10} Hz), radiowaves (up to 10^9 Hz), and the low and ultra-low frequencies, (10 Hz–10^3 Hz) and extremely low frequency (ELF) waves (3–10 Hz).

Bands in the lowest frequencies are of special interest. Known as Schumann Resonances (SR), they are EM waves that occur around 7.8, 14, 21, 26 and 34 Hz with variations of up to ±2 Hz. SR are caused by standing waves continuously traveling around the globe, fed by the low to ultralow portion of the EM emissions from lightning strikes around the world. They are standing EM waves reflected off the ionosphere and the Earth's surface as shown in Fig. 2, left; The SR are believed that to have been operating throughout Earth past and present during evolution of life as a constant background EM radiation field.

A number of studies have shown that EMF generated by electric devices have a demonstrable impact on health and/or behavior of humans and other organisms on Earth [1–5]. These effects are probably imparted through various biological mechanisms, many of which are yet to be understood or even identified. As we are

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Abbreviations

AC	alternating current
ATP	adenosine triphosphate
E	electric field
ELF	extremely low frequency
EM	electromagnetic
EMF	electromagnetic field
GSH	glutathione
GSSG	glutathione disulfide
LEET	low energy emission therapy
NAT	N-acetyltransferase
RF-EMF	radiofrequency electromagnetic field
SLF	super low frequency
SR	Schumann resonances
SWS	slow wave sleep
ULF	ultra low frequency
VLF	very low frequency

increasingly surrounded by new sources of EMF, it is important to review the state of knowledge of the effects of EMF on essential biofunctions and biorhythms such as sleep. Of particular interest are those frequencies which most closely mimic or interact with the background SR at which evolution has occurred, since it is possible that these EMF generated at these frequencies have unique impacts on biology.

Characteristics of electromagnetic fields

Electromagnetic fields may be characterized according to their wave frequency – inversely related to wavelength - with lower frequencies having longer wavelengths and vice versa. EM waves can be described as an oscillating electric field (E) as well as an oscillating magnetic field (B), perpendicular to the electric field. Additionally, EM waves may be described by their photon energy, E, which is directly proportional to frequency; for example, ionizing radiation such as gamma waves (10^{20} Hz) have the highest photon energy (1.25 MeV), whereas visible light (10^{14}–10^{15} Hz) has one millionth this energy (1.24 eV).

The interaction of EMF with matter, both living and non-living, depends on the characteristics of the energy of the fields themselves. For example, high energy, ionizing radiation imparts enough energy to electrons to knock them off their bound states; whereas lower energy, non-ionizing radiation can couple to electrons and to protons and atomic nuclei, thereby exerting opposite forces via their electric and magnetic field components. At the frequencies of visible light, protons and atomic nuclei are too heavy to respond to rapidly changing EMF, but electrons do interact with the electric fields inherent in these waves. These characteristic differences impart very different effects on matter, and predicate the unique influences of EMF in nature.

The magnetic components of any EM radiation are also an integral part of EMF. They too have distinct, important interactions with matter. Because any moving charge in a steady magnetic field, or any stationary charge in a variable magnetic field, will experience a force, there is potential for atomic and molecular alteration of substrates in ways that may impart biological impacts.

The scope of interactions of EMF with matter, in particular living matter, is rich and diverse, both as a function of frequency or wavelength, and of applied intensity. Studying their effects on biological processes requires simultaneously an open-minded and a cautious approach.

The potential for biological impact

Starting with frequencies of infrared light and lower, around 10^{13} Hz, electrons, protons and other atomic nuclei can all be influenced by varying EM fields. Atomic bonds can be stretched and deformed; and oxidation – reduction (redox) reactions can be initiated, in which an electron from one atom or group of atoms moving electrons from one atom or group of atoms to another, causing one to become chemically reduced and the other to become oxidized. This has implications for the metabolic cycle, a classical redox reaction, which is the fundamental biochemical process that controls the timing of all biochemical reactions in living cells, including energy production, RNA transcription, and DNA replication.

The impact of timing is conceptually critical. Through temporal coordination, a chemical conflict between the reductive and oxidative reactions is avoided, while at the same time a coherent or interfering transfer of energy is enabled between the ambient natural EMF and living cells. EM waves are time-dependent phenomena: their effects on temporally organized biochemical cycles in living cells, such as the reduction oxidation cycle, can generate quite opposite effects depending upon their phase relationships. The interaction between EM waves and electron transport in redox reactions clearly depends on the phase relationship between oscillating systems.

Whether or not EMF are able to affect biorhythms - including sleep – is also predicated on resonance, which occurs when the

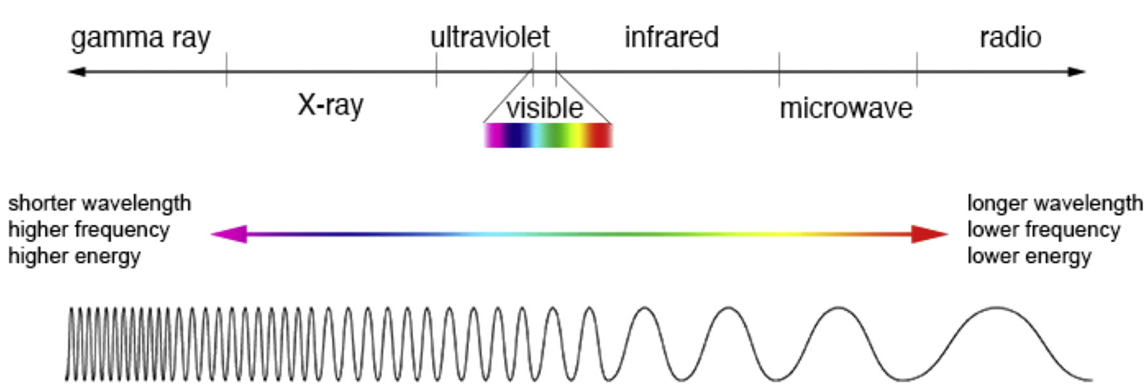

Fig. 1. The interaction of solar radiation with the earth's atmosphere generates an electromagnetic (EM) spectrum, of which visible light is only a small part [https://imagine.gsfc.nasa.gov/Images/science/EM_spectrum_compare_level1_lg.jpg].

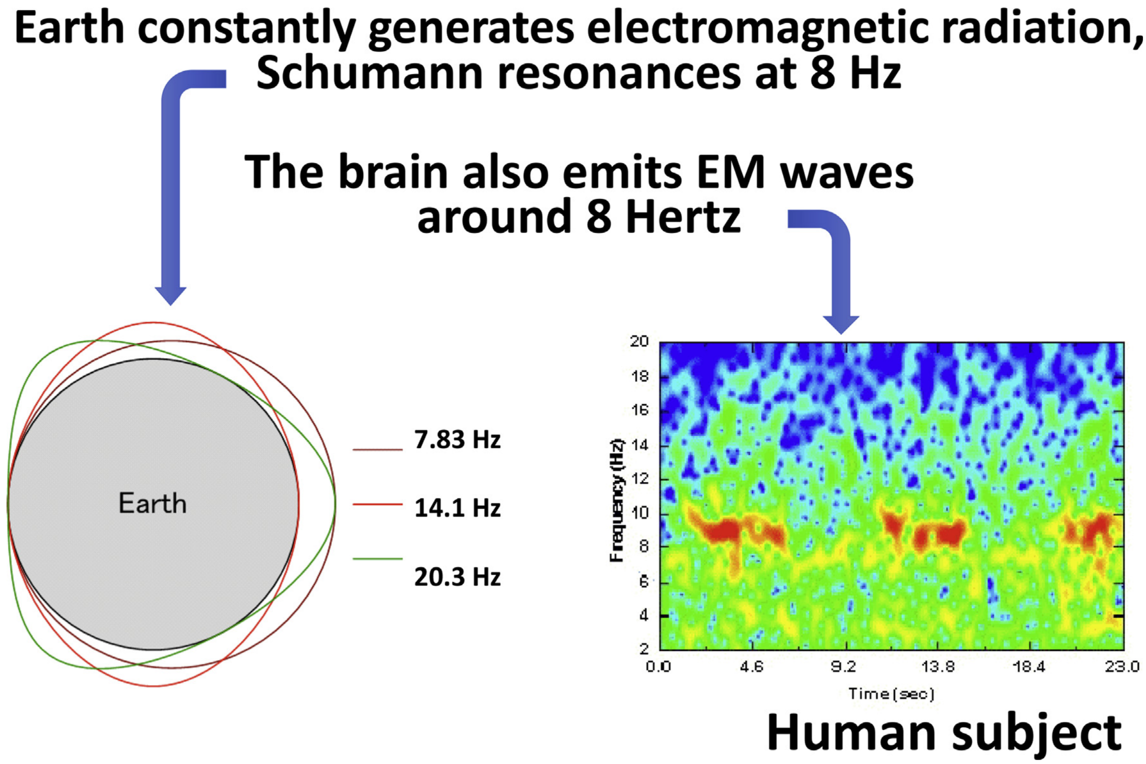

Fig. 2. Schumman Resonances and brain alpha waves.

cellular physiology is able to transfer energy from ambient EMF in tune with the electromotive force across membranes. Although the earth's geomagnetic field as well as man-made EMF in the environment are weak and generally thought to be masked by thermal fluctuations and other noise, the biophysical mechanism for EM perception is based on coherent quantum effects of extremely weak magnetic fields on the electron spin in each of radical pair intermediates of molecules in redox reactions [6]. Depending on the electron spin state, different reaction results are produced, and at different rates. The switch between the products of the redox reactions is shifted by the ambient EMF, which thereby would have implications for biorhythms [6].

Microwave and radiofrequency EMF (RF-EMF) in the GHz to MHz range, 10^9–10^5 Hz, may also be impactful on biological systems by straining molecular units and affecting their rotational and vibrational modes. Even at ultralow frequencies (ULF; 300 Hz–3 kHz), physiologically important molecular movements in biological systems are thought to be affected by EMF. The passage of ULF waves has been shown to impact rotating subunits of ATP synthase enzyme, which functions critically in cellular energy production. Indeed, the rotational frequencies of ATP synthase have been observed to coincide with certain ULF waves in the natural environment, giving rise to speculation of evolutionary integration of background frequencies into core biological processes.

One potential importance of ULF and ELF waves, and especially the SR, in the biological context is that they can potentially influence the natural electrical activity that is present in the nervous system and other organs able to generate electrical impulses in this range. In fact, it may well be that life has adapted in very specific ways to the influence of the ambient ULF/ELF waves by affecting temporal oscillations between oxidized and reduced metabolic states, which are responsible for various biorhythms, including the diurnal sleep cycle. SR themselves vary with respect to intensity and frequency, in a diurnal cycle due to the rotation of the Earth, by the moon's gravitational forces, which act on the Earth's atmosphere and ionosphere, by solar events leading to geomagnetic storms, and by cosmic events such as X-ray and gamma-ray bursts.

Consideration of EMF influence on biology, then, must take into account the essential dependencies on several critical variables, including frequency and energy intensity, temporal coordination, and resonance with biological mechanisms. By contrast to the natural phenomena which contribute to EMF, man-made sources of EMF have greatly augmented the frequencies and intensity to which humans and other organisms are exposed. Man-made EM radiation emanates from the production, transmission and utilization of electricity (power transmission lines, home wiring, motors, generators), wired and wireless electronics (televisions, radio, computers, cell phones, WI-FI), as well as medical devices (MRI). Increasingly, in the era of "smart" cars, homes, watches, and more, man-made EMF are omnipresent in everyday environments. Exposure to manmade EMFs ranges in frequency from super low frequency (SLF) as in the case of power lines and AC currents (50–60 Hz), to very low frequency (VLF) as in the case of computers (60–100 kHz), to high frequency as in the case of cellphones and other wireless communication devices (1.9–2.2 GHz), to ionizing radiation as X-rays from artificial radioactive materials and medical devices (30×10^{16} Hz). Acknowledging the potential for very different biological impacts along the frequency spectrum, this review particularly focusses on studies evaluating potential human impacts of SLF (50–60 Hz), and ELF (4–20 Hz) EMF bands.

Methodology

The articles utilized in this review included only peer-reviewed original studies published between 1990 and 2018 and written in English. A systematic search of literature was conducted using databases including PubMed Central, ISI Web of Knowledge, and Google Scholar. Search terms were "Electromagnetic field" with "sleep" or "polysomnography". The search returned a total of 257 peer-reviewed articles. In addition, references cited in retrieved articles were screened for additional reports.

Articles published using the same sample were counted as a single study although information to describe the sample and methodology could come from different articles associated with that specific study sample.

Results

Evidence of biological impact

Radiofrequency (10 MHz–300 GHz)

Most of the studies of EMF on human health and biology have evaluated RF. While these studies have been reviewed elsewhere [7,8], generally speaking, the amplitude of the RF-EMF fields is often selected to simulate the radiation emitted by cellular phones near the human body, emulating conditions in which a cell phone is held close to the head for an extended period of time. The RF-EMF radiation to consider can be either pulsed (for example one burst every 5 s) or continuous (for specific periods of time or through the night). EEG generally, and sleep specifically, have been outcomes of interest, and studies that have examined the effects of these radiations on EEG and sleep structure are summarized in Table 1. Some of these studies demonstrate modest effects in EEG and sleep characteristics, but these are not consistent across studies. The effects from RF-EMF on sleep architecture vary considerably across studies, likely highly dependent on individual sensitivity, exposure, sample size and ambient EM conditions.

A few studies have sought to assess sleep impacts of man-made EMF in real-life conditions. Real life, non-laboratory, human studies conducted to date have not been able to demonstrate unequivocally the presence of negative effects of RF-EMF on sleep architecture. Independent surveys inquiring populations living at various distances from RF emitting stations about their sleep quality and sleep disturbances [9–12] have suggested that the reporting of negative symptoms was biased by the presence of concerns of the individuals about the radiation emitted by the emitting stations, i.e., those people that were most concerned about the presence of a mobile base station were the ones that were most likely to report a sleep problem. Indeed, perceived exposure has an important role in symptom reporting [13,14], complicating interpretation of such studies. In Mohler and colleagues' prospective cohort study of 955 adults, exposure to environmental RF-EMF did not affect self-reported sleep quality [15]. Interestingly, a naturalistic study of 2361 seven-year old children with measured exposures to RF-EMF in the school and home environments, as well as parentally reported time spent with mobile and cordless phones, did not find an association between RF-EMF exposures and sleep quality; however, higher mobile phone usage itself was associated with less favorable sleep duration, night awakenings, parasomnias, and bedtime resistance [16].

Super low frequency (30–300 Hz)

Exposure to EMF with a frequency of 50 Hz (e.g., in Europe) or 60 Hz (e.g., in North America) generated by the electrical power grid and electrical devices is ubiquitous. The international guidelines for limiting exposure to time-varying electric and magnetic fields in the low-frequency range consider ULF and ELF EM fields to be biologically relevant only if their amplitudes exceed the ambient field by at least 109 times [17]. Since the intensity of the SLF fields is about 10–40 pT, only radiation in excess of about 10–40 mT magnetic flux density would have to be considered. This value needs to be put in perspective with the intensity of the Earth's prevailing magnetic dipole field, which ranges from 25 to 65 μT depending on the latitude.

Because of the ubiquity of 50–60 Hz EMF, influence of sleep on this band has been evaluated. Åkerstedt et al. evaluated the effects of a 50 Hz EMF on the sleep of 18 healthy good sleepers (8 F, 18–50 y.o.) [18]. The subjects were asked to sleep overnight in a wooden cabin where they were blindly exposed to a 1 μT field generated by 50 Hz AC or in neutral conditions, one week apart. Background EMF, light and noise were controlled. Exposure to EMF resulted in disturbed sleep, with statistically significant reductions in total sleep time, sleep efficiency, SWS in stages 3 and 4, and slow wave activity. Graham and Cook evaluated the effect of an intermittent and continuous circularly-polarized, sinusoidal 60 Hz magnetic with a flux density of 28.3 μT on sleep EEG of 46 healthy volunteers (22 Men, 24 women, aged 40–60 y) [19]. In this experiment only the intermittent exposure resulted in disrupted sleep, and was associated with reductions in total sleep time, sleep efficiency, REM sleep, and increased time in stage 2 sleep. Recently, Hosseinabadi and colleagues reported on a group of 132 power plant workers in comparison to 143 other workers and found a dose-dependent relationship between exposure to EMF and lower sleep quality as measured by the Pittsburgh Sleep Quality Index Questionnaire [20].

EMF influence on melatonin has been a particular area of interest. As detailed earlier, EMF have the potential to influence chemical reactivity and the redox potentials. The redox state of melatonin is critical for its function in diurnal timekeeping. By acting as an antioxidant, melatonin increases the ratio of reduced to oxidized glutathione GSH/GSSG, which drives the period of the metabolic cycle and hence the diurnal phase of the sleep-wake cycle [21]. A "melatonin hypothesis" was proposed to implicate SLF-EMF exposure in risk for a variety of reported health impacts including sleep quality, stress, depression and anxiety, and cancer, though direct evidence is scant [22]. Early investigations of exposure focused on electric fields with studies demonstrating reduction of pineal melatonin and N-acetyltransferase (NAT), the key enzyme for melatonin synthesis, in mice exposed to electric fields for 20 h/d for 30 d [23,24]. Later investigations of magnetic fields on murine melatonin resulted in mixed and inconsistent results [17]. Human studies, too, are limited. Experimental exposures tend to be short-term and in healthy volunteers, so data from occupationally exposed individuals may provide additional insight.

Studies by Burch and colleagues have observed a decreased excretion in urine of 6-OHMS, a melatonin metabolite, among 142 electrical utility workers, who were exposed to magnetic fields with a frequency of 60 Hz [3,25]. Effects on 6-OHMS excretion in urine, taken at the end of their shift, were detected on the second day of exposure on workdays. However, this decrease was also modulated by light exposure: workers with low workplace lights exposure had a progressive decrease in mean 6-OHMS concentrations whereas those exposed to high ambient lights had negligible changes. The type of EMF - circular, elliptical or linearly polarized - also influenced the decrease in the urinary 6-OHMS excretion [25]. Workers stationed near energized 3-phase conductors (polarized circular or elliptical magnetic fields) had lower nocturnal and post-work 6-OHMS/creatinine concentrations compared to those with 1-phase exposure (polarized linear magnetic field).

Another study has investigated the effects of exposure to 16.7 Hz magnetic fields on 6-OHMS excretion among 108 railway workers [26]. Excretion levels were compared between workdays and leisure days for morning and evening urine collections. It was found that compared with leisure days, workers exposed to higher EMF

Table 1
Effects of RF-EMF radiation on sleep.

Authors	N of subjects	EMF Frequency & Intensity	Exposure length	#nights	Design	Effects of EMF on sleep
Mann et al., 1996 [4]	12 healthy M (21–34 y.o.)	RF, 900 MHz I: 0.05 mW/cm^2	Continuous all night exposure	3 successive nights	Double-blind, Crossover	• Decreased sleep latency • Decreased REM (% TST) • Increase in the mean power density during REM • Modifications of the alpha$_1$ and alpha$_2$ bands
Wagner et al., 1998 [48]	24 healthy M (18–37 y.o.)	900 MHz	Continuous all night exposure	2 nights: one with EMF exposure; one without EMF exposure	Double-blind, Crossover	• Decrease in REM duration (trend) • Increase in REM latency for the first episode (trend) • No change in the spectral power
Borbely et al., 1999 [49]	24 healthy M (20–25 y.o.)	900 MHz	15- minute intervals- all night	2 nights of experimental conditions, one-week interval	Double-blind, crossover	• Decreased WASO • No effect on REM sleep • Enhancement of the first non-REM sleep episode spectral power
Akerstedt et al., 1999 [18]	8 F & 10 healthy M (18–50 y.o.)	50 Hz	Continuous all night exposure	2 nights experimental conditions, one week apart	Double-blind, Crossover	• Reduced TST • Reduced Sleep Efficiency • Reduced SWS • Reduced SWA • Lower rated sleep depth
Graham & Cook, 1999 [19]	24 healthy M (18–33 y.o.)	60 Hz I: 28.3 μT C: Circular	1) Continuous exposure 2) intermittent exposure (1 h on (intervals of 15 s)/ 1 h off)	3 separate nights one week apart	Double-blind, crossover	No significant effect of EMF continuous exposure on the sleep architecture. Intermittent exposure: • Decreased TST • Increased WASO • Decreased SE • Increased Stage 2 (% TST), • Decreased REM (% TST) • Increased REM latency
Wagner et al., 2000 [50]	20 healthy M (19–36 y.o.)	900 MHz SAR: <10 W/kg Pulse C: Circular	Continuous all night exposure	2 nights experimental conditions, one week apart; total four nights	Double-blind, Crossover	• No significant changes in sleep parameters • No significant changes in the spectral power (Delta, Theta, Alpha, Beta)
Huber et al., 2000 [51]	16 healthy M (20–25 y.o.)	A: 900 MHz SAR: 0.14 W/Kg Pulse Linear	30 min prior to a 3-h sleep episode in the late morning	one morning	Double-blind, Crossover	• No significant changes in sleep parameters • Changes in the spectral power in NREM: Increase in the 9.75–11.25 Hz and 12.5–13.25 Hz band
Huber et al., 2002 [52]	16 healthy M (20–25 y.o.)	A: 900 MHz SAR: 1 W kg^{-1} Pulse 1 night/ continuous 1 night	30 min prior to night-time sleep	3 nights experimental conditions: 1 pulse, 1 continuous, 1 sham	Double-blind, Crossover	• No effect of EMF exposure on the sleep architecture. • Spectral analyses showed an increase in the spindle amplitude in the pulse modulated EMF in waking before sleep onset and in stage 2 sleep
					Double-blind, Crossover	

Loughran et al. 2005 [53]	27 healthy M and 23 F (27.9 ± 10.9 y)	A: 894.6 MHz SAR: 0.11 W/kg T: Pulse C: Linear	30 min prior to night-time sleep	2 nights experimental conditions, one week apart		• Decrease in REM latency following EMF exposure • Significant enhancement of the EEG power density in the 11.5–12.25 Hz frequency range following EMF exposure during the first 30 min of the first non-REM period.
Hinrichs et al., 2005 [54]	12 W and 2 M Volunteers	GSM 1800-type EMF I: 30 V/m SAR: 72 mW/kg T: Pulse of 1736 Hz C: Linear	Continuous all night exposure	4 nights of experimental conditions	Double-blind, Crossover	• No effect of EMF exposure on the sleep architecture. • No significant changes in the spectral power (Delta, Theta, Alpha, Beta1)
Altpeter et al., 2006 [9]	33 F and 21 M	A: 6.1–21.8 MHz (Shortwave radio transmitter)	24-h exposure	one week before the shutdown of the transmitter and one week after	Natural environment study	• Increase in morning tiredness with the increase in the EMF values • Decrease in melatonin excretion by a factor of 0.90 for every 1 mA/m increase in the magnetic field
Fritzer et al. 2007 [55]	10 healthy M EMF (22–36 y.o.) 10 healthy M – SHAM (23–37 y.o.)	A: 900 MHz I: 1 W/kg T: Pulse C: Linear	Continuous all night exposure	6 consecutive nights of experimental conditions	Double-blind	• No effect of EMF exposure on the sleep architecture • No significant changes in the spectral power (Delta, Theta, Alpha, Beta)
Regel et al., 2007 [56]	15 healthy M (20–26 y.o)	I: 0.2 or 5 W/kg^{-1}	30 min prior to sleep	3 nights of experimental conditions, one-week interval	Double-blind, crossover	No effect of EMF exposure on the sleep architecture Dose-dependent increase in the spindle frequency range in non-REM sleep
Leitgeb et al., 2008 [38]	43 Volunteers (17 M, 26 F)	A: 80 MHz to 2.5 GHz	Continuous all night exposure	Done at the home of the volunteers: 9 consecutive nights	Crossover natural environment. 3 conditions: 1) EMF unshielded control 2) true EMF shield and 3) sham-shield	• No significant effect of EMF exposure on the sleep architecture. • 16% of subjects (n = 9) had significant positive changes under sham-shield condition. • Four volunteers had deteriorated sleep under shielded condition (vs. unshielded condition)
Danker-Hopfe et al., 2011 [12]	30 healthy M (18–30 y.o.)	A: 900 MHz and 1966 MHz T: pulse	Continuous all night exposure	9 nights experimental conditions	Double-blind, Crossover	• Decreased Stage 2 • Increased REM sleep
Lowden et al., 2011 [57]	27 F & 21 healthy M (18–44 y.o.)	A: 884 MHz RF signal	3 h exposure before sleep	one night experimental condition	23 subjects with GSM mobile phone-related symptoms 25 non-sensitive subjects Double-blind study	• Increased Stage 2 • Decreased Stage 4 • Decreased Stage 3 + Stage 4 • Increased latency Stage 3 • Increase in the EEG alpha range • No effect on sleepiness • No difference between subjects with phone-related symptoms and non-sensitive subjects
Schmid et al., 2012 [58]	25 healthy M (20–26 y.o.)	A: 900 MHz RF EMF A: 900 MHz EMF	30 min prior bedtime	3 exposure nights separated by one week	Double-blind, Crossover	• No significant effect of RF EMF and EMF exposure on the sleep architecture.

(continued on next page)

Table 1 (*continued*)

Authors	N of subjects	EMF Frequency & Intensity	Exposure length	#nights	Design	Effects of EMF on sleep
		I: 2 W kg^{-1} T: Pulse				• Spectral power analyses showed increases for RF EMF in both NREM and stage 2 sleep
Lustenberger et al., 2013 [59]	16 healthy M (18–21 y.o.)	A: 900 MHz I: 0.15 W/kg T: Pulse Circular	Continuous all night exposure	two night experimental conditions	Double-blind, Crossover	• Decrease of 9 min in TST • Increase of 6.6 min is WASO • Spectral power: higher SWA in the 4th NREM sleep episode
Nakatani-Enomoto et al. 2013 [60]	7 F & 12 Healthy M (22–39 y.o.)	A: 1950 MHz I: 1.52 and 0.13 W/kg T: Continuous	3 h exposure before sleep with 5 min break every hour	two night experimental conditions	Double-blind, Crossover	• No significant effect of EMF exposure on the sleep architecture. • No significant changes in the spectral power (Delta, Theta, Alpha, Beta)
Lustenberger et al., 2015 [61]	20 Healthy M (23.3 ± 0.5 y.o.)	A: 900 MHz RF I: 2 W/kg T: Pulse	30 min prior to sleep	two night experimental conditions two weeks apart	Double-blind, Crossover	• No significant effect of EMF exposure on the sleep architecture. • Delta-theta activity higher under EMF • No difference in spindle activity • No « time » effect of EMF exposure

A: Amplitude; RF: Radio frequency; I: Intensity; T: Type; SWA= Slow Wave Activity; SAR: Specific Absorption Rate.

(20 μT) had a lower 6-OHMS/creatinine urine concentration in the evening urine sample while low magnetic field exposure did not affect 6-OHMS levels.

Aside from occupational exposure, residential exposure has also been studied. In an investigation of exposure to a 60 Hz magnetic field in the bedroom, Davis et al. found that such exposure lowered nighttime urinary concentration of 6-OHMS in 203 women, especially among women using beta blocker, calcium channel blocker, or psychotropic medications, which are known to affect melatonin levels [27]. Variable effects based on time of day have not been fully investigated but in a study 60 women, Juutilainen and Kumlin found that exposure to a 50 Hz magnetic field during daytime may enhance the effects of nighttime light exposure and decrease melatonin production [28].

However, several studies did not find any effects of SLF magnetic fields on melatonin secretion. Three epidemiological studies showed no effect of the exposure to SLF magnetic fields on melatonin secretion [29–31]. Gobba et al. noted similar levels of 6-OHMS excretion in two groups of workers exposed to magnetic fields ≤0.2 ??T and >0.2 ??T [29]. No association between residential exposure to a 60 Hz magnetic field and 6-OHMS excretion was observed in adults aged 50–81 y [30]. A study carried out on 50 electronic equipment service technicians, exposed to different kinds of fields, found significantly decreased levels of serum melatonin compared to the control group [31]. Touitou et al. showed that the long-term exposure to ELF-MFs did not change the level and diurnal secretion of melatonin [31]. These data suggest that magnetic fields do not have cumulative effects on melatonin secretion in humans.

In contrast to ELF-EMF, much less attention has been paid in epidemiological studies to the effects of intermediate frequency range (300 Hz to <10 MHz) and radio frequency range (10 MHz–300 GHz) EMF on melatonin. While no changes in urinary 6-OHMS excretion in women residing near radio and television broadcasting transmitters were found [32], Altpeter et al. reported that exposure to a broadcast transmitter with short-wave EMF (6–22 MHz) reduced melatonin excretion by 10% in 54 volunteers living in proximity of the station, and that following the shutdown of the station the melatonin excretion rebounded, and the rebound effect was greater in poor sleepers [9]. Mixed effects have also been reported from mobile phone use, with one study demonstrating daily use of a mobile phone for more than 25 min decreased the level of melatonin secretion in electric utility workers also exposed to a 60 Hz ELF field [33].

Extremely low frequency (3–30 Hz)

There is an overall paucity of scientific investigations on the potential impacts of ELF-EMF on EEG and sleep; what is available focusses upon the potential utility of ELF-EMF as a therapy for insomnia. A few studies have investigated the possible application of EMF as treatment for insomnia using Low Energy Emission Therapy (LEET). One of the first studies evaluated the sleep EEG following a 15-min treatment with a 42.7 Hz amplitude-modulation of 27.12 MHz electromagnetic field administered through of a small monopole antenna in the form of a spoon that could be placed in the mouth of a subject. The double-blind cross-over experiment was performed in 52 healthy adults (32 F, aged between 18 and 53) and resulted in a decrease in sleep latency, longer duration of stage 2 sleep, and deeper sleep following the active treatment [34]. Pasche et al. performed a follow-up study with 97 patients suffering from psychophysiological insomnia, who were treated for 20 min, three times per week for four weeks in a double-blind, randomized placebo-controlled study design. The LEET device used had a set of four amplitude-modulated frequencies that were selected specifically for the treatment of insomnia. The bandwidth of the modulated frequencies ranged between 0.1 Hz and 10 kHz. In patients receiving the active treatment, a rise in total sleep time, a decrease in sleep latency, and 30% increase in number of sleep cycles per night were observed. Pasche and colleagues concluded that this treatment might benefit people suffering from chronic insomnia [35]. In a study by Kelly and colleagues, LEET was not shown to alter melatonin circadian rhythm or cognitive performance in a shift work model [36]. Pelka et al. also reported clear relief of insomnia symptoms in a blinded, placebo-controlled study of sleeping with a device in proximity to the head which emitted a pulsed magnetic field at a frequency of 4 Hz and with a high intensity of 5 μTs. After four weeks, all the active treatment patients reported improvement in all or part of the sleep quality parameters, while the placebo patients reported little or no improvement [37]. These studies suggest the possibility of a therapeutic use for EMF to target certain sleep-wake perturbations, though more work is needed in this area.

Studies like those reported by Pelka et al. [37] demonstrate that exposure to EM waves in the ELF range can have a beneficial effect on patients suffering from insomnia. However, there are also numerous reports that periods of increased natural ULF EMF activity, such as during geomagnetic storms, are marked by increased levels of anxiety, irritability, insomnia, fatigue, restlessness, and a statistically significant upswing in the number of accidents, suicides and crimes [38–42]. Rather amazingly, a study of the worldwide performance of stock markets since the 1920s indicates that the stock brokers, who have to buy and sell shares, often under intense time pressure, perform less well on days of major geomagnetic activity than on days of no geomagnetic activity [43]. During geomagnetic storms, Earth is subjected to rapidly changing magnetic fields created in the ionosphere by the arrival of waves of solar wind stemming from gigantic plasma eruptions on the sun's surface. When the solar wind waves slam into the Earth's ionosphere, they create electric currents which can reach millions of amperes. The associated changes in the magnetic field produce powerful EM waves in the ULF range with intensities reaching 100–1000 nT, thereby exceeding the intensities of the SR by 4–5 orders of magnitude.

While there are no well-controlled experimental protocols evaluating such potential links, these observations raise questions regarding whether there is a causal link between ULF activity and reported effects on physiology and human behavior. Effects might be mediated by either EM radiation at discrete frequencies, or by broad-band white noise across the ELF/ULF spectrum. Potential mechanisms include impacts on the aforementioned SR. As indicated in Fig. 1, right, it is remarkable to note that the frequency of the EM waves released by the human brain during activity, falls into the range of the first SR, around 8–10 Hz. In fact, this is a universal feature common to all animals with a central nervous system. It suggests that life has evolved in the context of the SR and to possibly use them to regulate certain crucial physiological processes.

Seemingly disparate observations from the natural world regarding animal behavior before earthquakes may in fact suggest an underlying connection between exposure to ELF/ULF- EMF and mammalian behavior. In the case of earthquakes, processes deep in the Earth's crust linked to the build-up of tectonic stresses give rise to telluric currents, which can also reach millions of amperes. If these currents fluctuate, which they typically do, they likewise emit powerful EM waves. Only EM waves in the frequency range below 10–20 Hz can propagate tens of kilometers through the rock column and reach the Earth's surface. Observations made prior to large earthquakes indicate that animals can sense the approach of such natural disasters days before they strike. One striking example

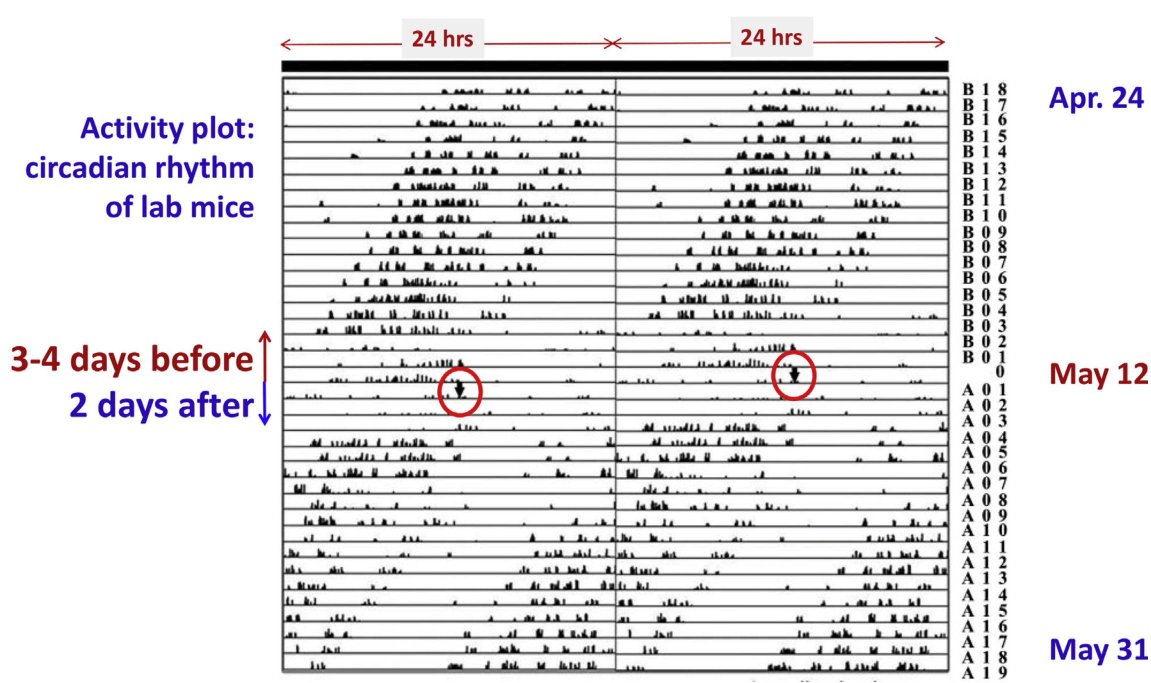

Fig. 3. Observations prior to the magnitude 8.0 Wenchuan earthquake that struck on May 12, 2008. When the mice were submitted to the 23 h day–night rhythm, they initially adjusted smoothly, adapting their circadian rhythm to the schedule as evidenced by their activity record. However, three days before the earthquake, the mice suddenly stopped moving around. After the earthquake they remained still for another three days but then slowly resumed their normal activity.

is seen in the perturbations of the circadian rhythm of laboratory mice in an experiment at the University of Chengdu, China, that had fortuitously been set up 19 d before the magnitude 8.0 Wenchuan earthquake that struck on May 12, 2008 only about 75 km away [44]. Fig. 3 shows that, when the mice were submitted to the 23 h day–night rhythm, they initially adjusted smoothly, adapting their circadian rhythm to the schedule as evidenced by their activity record. However, three days before the earthquake, the mice suddenly stopped moving around. After the earthquake they remained still for another three days but then slowly resumed their normal activity. At the same time the Chengdu Magnetic Observatory, located about 30 km from the epicenter of the earthquake, recorded unusual magnetic field variations as see in Fig. 4. Particularly strong was the z component of the magnetic field, which suggests powerful telluric currents flowing horizontally in the underground. The strong magnetic field variations, which these currents engender, most prominently during the last three days before this seismic event, are equivalent to intense ULF emissions, which permeated the entire region and must have been felt by the mice in the circadian rhythm experiment.

Another example of behavioral changes among animals, in this case wild animals in a tropical rainforest setting in a National Park in the Peruvian Andes, has been reported on the basis of objectively collected and evaluated photographic records [45]. Starting 20 d before a magnitude 7.0 earthquake, a 10 camera cluster, operating day and night with motion-triggered infrared flashes, recorded a decrease in the activity of mammals and ground-living birds with near-zero animals seen during the last seven days prior to the main shock. Authors noted that such a decrease in animal activity is highly unusual in a tropical rainforest setting.

Humans are also affected by local conditions before major seismic events. When a magnitude 7.6 earthquake hit a remote region in Southern Siberia of Russia in September 2003, it was preceded by a range of pre-earthquake phenomena in the physical environment. A review of medical records indicates that, 14 d before the event, the number of patients coming to the Emergency

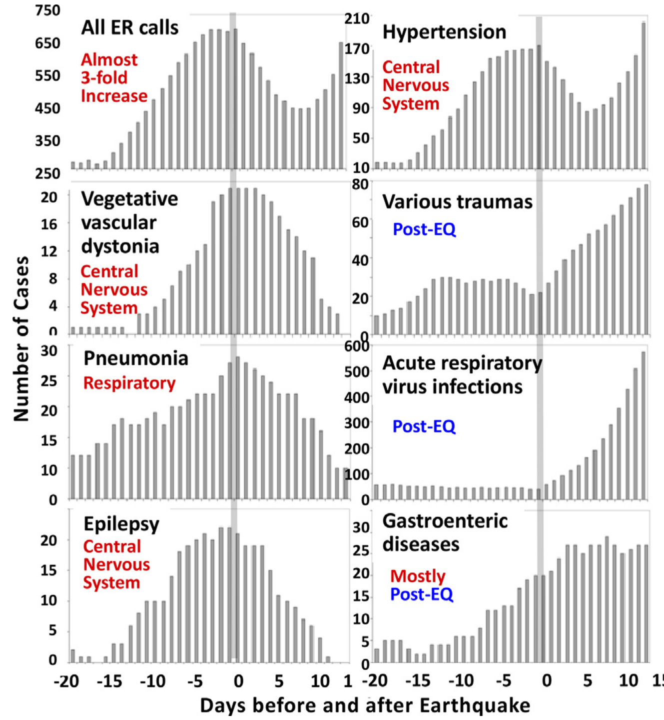

Fig. 5. Number of visits to the regional emergency rooms prior to and immediately after the M = 7.6 Chyua earthquake in southernmost Sibaria.

Rooms started to increase significantly, reaching 2.7 times the long-term average on the day before the earthquake [46]. Fig. 5 shows that CNS-related complaints, as well as pneumonia, most prominent among the medical conditions for which the patients sought help before the earthquake. No magnetic field records are available for this event. It has been speculated that the central nervous

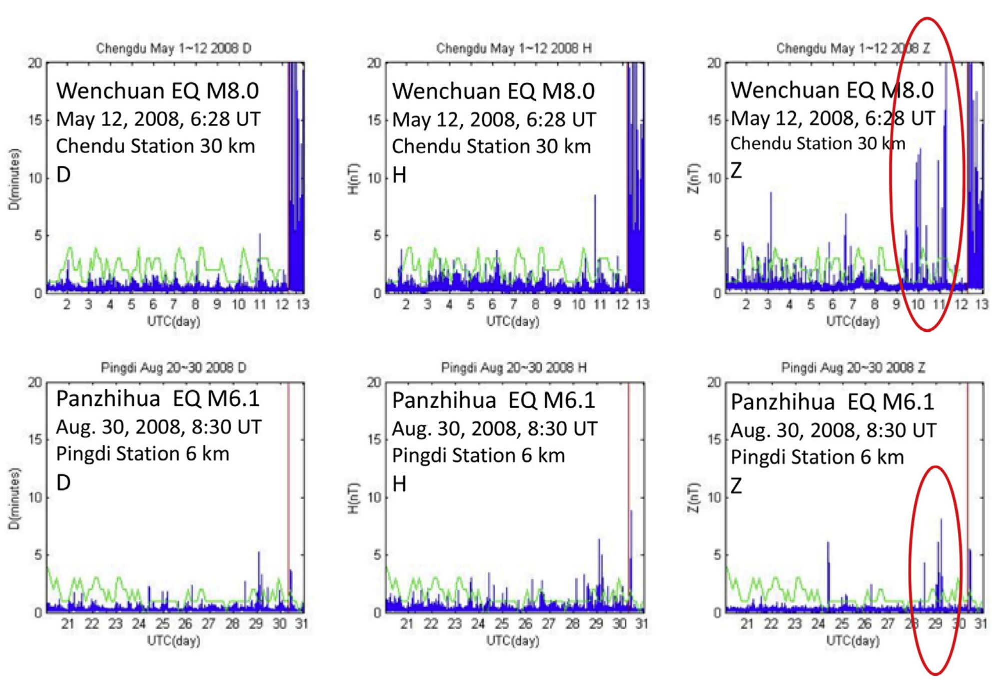

Fig. 4. Strong magnetic field variations most prominent during the last three days before the seismic event, are equivalent to intense ULF emissions.

system's susceptibility to alterations in background EMF are mediated by its dependence upon ATP energy metabolism. ATP synthase, the energy engine of most living organisms, is imbedded into the cell membranes of mitochondria. A characteristic feature of cellular ATP synthase is a rotational frequency in the ELF/ULF frequency domain, and the frequency of rotation is synchronized among the thousands, probably tens of thousands, of ATP synthase entities that form densely packed 2-dimensional quasi-crystalline arrays. Environmental EMF such as the Schumann resonances have been proposed to be an external “tuning fork” required to achieve synchrony in the rotation of the ATP synthase units, both in frequency and phase. If the SR provide this function, the observations reported above, in particular the perturbation of the ULF field by geomagnetic storms and local stress-activated telluric currents generated during the approach to major earthquakes would find a ready explanation [47].

Conclusion

Life has evolved in the context of Earth's extant EMF, and particular frequency ranges may be important for human health, behavior, and cellular function. As such, naturally occurring alterations in background EMF intensity, as well as the induction of artificial EMF generated from electrification and medical, communications, and consumer devices, have come to be considered environmental exposures, around a nascent which a medical literature has formed. While terminology varies, sleep architecture and electroencephalographic measures of sleep have commonly assessed variables of electricity- and device-generated EM exposures, as exposure-related sleep disturbance is a commonly cited complaint. Largely such investigations of EMF and sleep have been aggregated around EM higher radiofrequency bands, but emerging observations of exposures to alterations of environmental EMF in the ELF/ULF bands suggest that these low frequencies may have particular consequences for central nervous system function.

Effects from RF-EMF on sleep architecture vary considerably across studies. This inconsistency suggests a large individual variability, and more definitive conclusions may require studies with a greater sample size and real time measurements of ambient conditions, including the power spectrum of natural EM and metabolic cycle indicators such as oxygen consumption and heart rate variability.

There is some evidence suggesting that EMF may have an effect on sleep EEG, with reported pulse-modulated RF EMF effects on EEG power in alpha and beta or delta and theta bands when exposure occurs during sleep. However, no functional differences related to sleep have been identified, and perceived exposure has an important role in symptom reporting, which can bias data in real-world studies.

A review of the studies on the effects of EMF on melatonin secretion and sleep architecture shows that results are still inconclusive and often contradictory, perhaps because the phase relationship between the time-varying EM and the metabolic cycle-driven oscillations of melatonin are often not considered. Also, several factors other than EMF, such as age, might have a greater influence in modifying melatonin secretion but were rarely adequately controlled.

Finally, naturalistic observations regarding alterations in animal and human behavior in the face of sustained or large magnitude EMF changes remind that we have much yet to learn about how cellular and biological processes, sleep-wake, and human behavior may be impacted by exposure to changes in EMF background. Many questions remain open to discussion and a significant research effort is needed in this field to achieve clinically relevant understanding of the effects of industrial EMF on human biorhythms, including sleep.

Practice points

1. Electromagnetic fields are naturally occurring phenomena on earth;
2. Artificial electromagnetic fields, like RF-EMF, may sometimes have biological impacts on human functioning (biorhythms, melatonin secretion, sleep …) but the research remains inconclusive and often contradictory;
3. Therapeutic EMF, such as LEET, have shown promising results in helping those with insomnia but there is still a paucity of studies using LEET.

Research agenda

1. Effects of RF-EMF on sleep architecture need to be studied with better controlled studies (e.g., real time measurements of ambient conditions) and with larger samples.
2. The impacts of changes in EMF on cellular and biological processes (such as circadian rhythms) remain scarcely studied.
3. Clinical utility of therapeutic EMF on sleep disturbances should be further studied.

Conflicts of interest

The authors do not have any conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2019.06.001.

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