

Electromagnetic Waves and Human Health

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1. Introduction

Electromagnetic waves are produced by the motion of electrically charged particles. These waves are also called electromagnetic radiation because they radiate from the electrically charged particles. They travel through empty space as well as through air and other substances. Electromagnetic waves at low frequencies are referred to as electromagnetic fields and those at very high frequencies are called electromagnetic radiations (1,2).

2. Classification of electromagnetic waves

According to their frequency and energy, electromagnetic waves can be classified as either ionizing radiations or non-ionizing radiations (NIR).

Ionizing radiations are extremely high frequency electromagnetic waves (X-rays and gamma rays), which have enough photon energy to produce ionization by breaking the atomic bonds that hold molecules in cells together.

Non-ionizing (NIR) is a term for that part of the electromagnetic spectrum which has photon energies too weak to break atomic bonds. They include ultraviolet radiation, infrared radiation, radiofrequency and microwave fields.

NIR can not cause ionization however have been shown to produce other biological effects, for instance by heating, altering chemical reactions or inducing electrical currents in tissues and cells.

There are four subgroups of electromagnetic radiation fields with frequency and intensity. This electromagnetic spectrum begins at a frequency of 1 Hertz (Hz), which is 1 wave per second (1,2,3).

2.1 Static electric

Stationary electric charge that is built up on the surfaces and materials. Electric fields are associated with the presence of electric charge, magnetic fields result from the physical movement of electric charge. Human body can not feel less than 2000 volts of static discharge. Magnetic fields can exert physical forces on electric charges when charges are in motion. The magnetic flux density measured in teslas (T), is accepted as the most relevant quantity for relating to magnetic field effects (4). A summary of sources of exposure to static fields in Table 2.

| Type | Frequency range | Source |
|-------------------------------|--|--|
| Static | 0 Hz | Natural Video MRI Industrial electrolysis |
| Extremely low frequency (ELF) | ($0 < f \leq 300$ Hz), | Powerlines Domestic distribution Electric engines in cars, train and tramway |
| Intermediate frequency (IF) | $300 \text{ Hz} < f \leq 100 \text{ kHz}$ | Monitors, Anti theft devices in shops, Hands free access control systems, Card readers Metal detectors |
| Radio frequency (RF) | $100 \text{ kHz} < f \leq 300 \text{ GHz}$ | Broadcasting and TV; Mobile telephony Microwave oven Radar Portable and stationary radio transceivers, Personal mobile radio. |

*Adopted from: Possible effects of Electromagnetic Fields (EMF) on Human Health. Scientific Committee On Emerging And Newly Identified Health Risks (SCENIHR) 19 July 2006 MRI: Magnetic Resonance Imaging

Table 1. Classification and sources of electromagnetic radiation fields*.

| Sources | flux density |
|----------------------------------|--------------|
| Typical electric fields | |
| Video Display Unit, Tv | 20 kV/m |
| Under 500 Kv Transmission Line | 30 kV/m |
| Atmospher | 12-150 V/m |
| Typical magnetic fields | |
| Geomagnetic Field | 0,03-0,07 mT |
| Magnetic Resonance Imaging (MRI) | 2,5 T |
| Industrial DC Equipment | 50 mT |
| Small Bar Magnets | 1-10 mT |
| Magnetic Levitation Train | 50 mT |

Table 2. Sources of exposure to static fields and their flux densities.

2.2 Extremely Low Frequency (ELF)

Extremely low frequency is a term used to describe radiation frequencies below 300 Hertz (Hz). ELF fields are oscillating fields and very important for public health because of the widespread use of electrical power at 50-60 Hz in most countries (1,5).

2.3 Intermediate Frequency (IF)

Intermediate Frequency is a term to describe radiation frequency between 300 Hz and 100 kHz. There are experimental and epidemiological data from the IF range. Therefore, assessment of acute health risks in the IF range is currently based on known hazards at lower frequencies and higher frequencies. Proper evaluation and assessment of possible health effects from long term exposure to IF fields are important because human exposure to such fields is increasing due to new and emerging technologies. Typical examples are: computer and tv screens with use cathode ray tubes, compact fluorescent lamps, as well as radio transmitters, anti theft devices in shops, hands free access control systems, card readers and metal detectors. It is also used in electrosurgery (1,2).

2.4 Radio Frequency (RF)

RF includes the frequencies between 100 kHz and 300 GHz of the electromagnetic spectrum. RF sources are widespread used in whole world. Majority examples are mobile phones, broadcasting, medical and industrial applications. The RF sources are used in different frequency bands and subdivided in different categories:

2.4.1 Sources operated close to the human body

Main examples of this type are mobile RF transmitters. One of the examples is mobile phones; more than 1.5 billion people are using mobile phones worldwide. In addition to mobile phones, other wireless applications like cordless phones, e.g. DECT, or WLAN systems are very common. The maximum peak power level of a DECT system is 250 mW, of a WLAN system 200 mW.

2.4.2 Sources operated far away from the human body

Such sources are fixed installed RF transmitters. An example is base stations that are an essential part of mobile communication networks.

2.4.3 Medical applications

Some medical applications use electromagnetic fields in the RF range. Therapeutic applications such as soft tissue healing appliances, hyperthermia for cancer treatment, or diathermy expose the patient well above the recommended limit values to achieve the intended biological effects (1,5).

3. Effects on biological systems of electromagnetic fields

In 1935 Burr and Northrop examined and published the effects of stable voltage gradients on various biological systems. They were followed by a lot of scientists who found that stable voltage gradients led to many drastic changes in the organism, including growth and local injury. Studies have shown that these effects were associated with changes in distribution of ions (6).

According to some authors, there is connection with electromagnetic fields and disappearance of bees known as colony collapse disorder in Europe and the US, and that it could also interfere with bird migration (7,8).

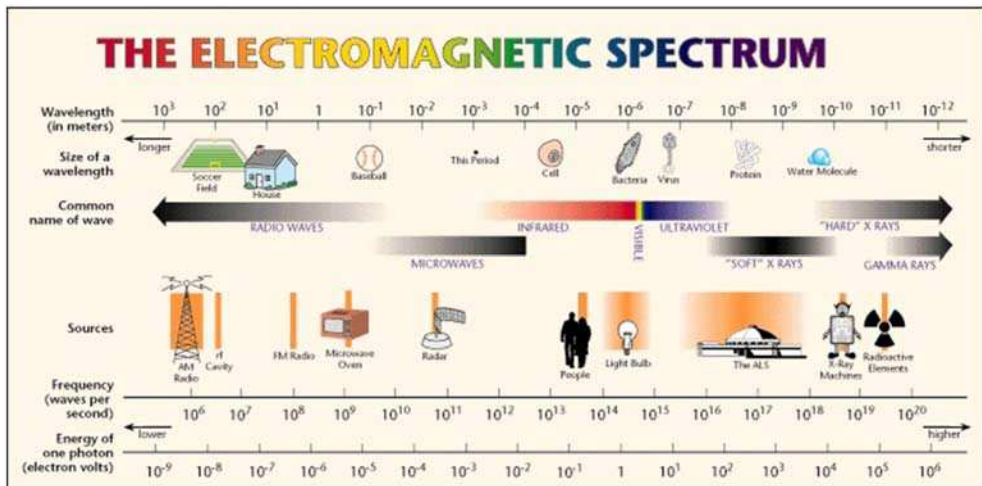


Fig. 1. The Electromagnetic waves spectrum. Adopted from Electromagnetic cellular interactions Cifra M, Fields JZ, Farhadi A.

4. Effects of human health

While the positive aspect of technologic innovation makes the life easier, it may also involve components that impair the quality of life via its certain negative effects. A discussion about the adverse effects of electromagnetic waves on the biological life has been ongoing since the discovery of electricity in the 19th century (6).

Electromagnetic waves generated by many natural and human-made sources can travel for long distances and play a very important role in daily life. In particular, the electromagnetic fields in the Radiofrequency (RF) zone are used in communications, radio and television broadcasting, cellular networks and indoor wireless systems. Resulting from the technological innovations, the use of electromagnetic fields gradually increases and thus people are exposed to electromagnetic waves at levels much higher than those present in the nature (1,2,5). Along with the widespread use of technological products in daily life, the biological effects of electromagnetic waves started to be discussed.

Particularly, the dramatically increasing number of mobile phones users rise significant concerns due to its potential damage on people exposed by radiofrequency waves.

Since mobile phones are used in positions very close to the human body and require a large number of base station antennas, the public and the scientists have question marks in their mind about the impact of mobile phone networks on health (9).

4.1 Evidence for cellular effects of electromagnetic fields

The general opinion is that there is no direct evidence of hazardous effects on human health incurred by low-frequency radiofrequency waves. Studies at the cellular level, which uses

relatively higher frequencies, demonstrate undesirable effects (10-11). Some studies revealed that different dimensions of electromagnetic waves have not shown any DNA damage on different cell lines. For example, in a comprehensive review published, Brusick et al have reported no evidence regarding the direct mutagenic effect of radiofrequency signals on cells (12).

On the other hand, there are a lot of contrary study published in recent years. Most of them concerned about evidence of biochemical or cellular effects of electromagnetic fields. Marino and Becker have shown that static or very low-frequency electromagnetic fields may lead to biological effects associated with redistribution of ions. Furthermore, many studies demonstrated that biological effects of low-frequency magnetic fields may penetrate into deeper tissues (13).

Foletti et al. showed that ELF-EMF may have an effect on several cellular functions such as cell proliferation and differentiation, which was followed by many other researchers such as Tian et al. who showed its effect on apoptosis, Takahashi et al. on DNA synthesis, Goodman et al. on RNA transcription, Goodman and Henderson on protein expression, Zrimec et al. on ATP synthesis, Paksy et al. on hormone production, Kula et al. on antioxidant enzyme systems, Milani et al. on metabolic activity, and Wolf et al. on NF κ B and cell destruction (14,15,16,17,18,19,20,21,22,23).

Giladi et al. demonstrated that EMF of intermediate frequency was effective in arresting the growth of cells. Kirson et al. indicated that this direct inhibitory effect on cell growth can be used for therapeutic purposes in the treatment of cancer (24,25).

EMF of very high frequency has thermal and non-thermal effects on the biological systems. This thermogenic effect is mainly associated with the intensity of EMF, which is expressed as specific absorption rate (SAR). Thermal effect or increased temperature lead to various changes in the cellular functions, which may result in cell destruction (26,27,28). Morrissey et al. showed that biological effects may occur even at very small temperature changes in in-vitro experimental models (29).

There are many papers showing that a weak EMF has no significant effect on biological systems. However, it appears that these studies have a poor design in general, and they lack appropriate control groups, and they are also accompanied by confounding factors (27,30).

The fact that no significant evidences were detected in the above epidemiological trials supporting the suspicions that exposure to electromagnetic waves could result in cancer is in line with the in vitro studies. The effects of electromagnetic fields on different cell lines were studied in the last 30 years and no evidence on their direct or indirect DNA damage were detected. Maes (31) and Vijayalaxmi (32) exposed peripheral blood cells to 935 and 2450 MHz electromagnetic field and reported no DNA damage in cells after 2-hours periods. Malyapa studied the effects of 2450 MHz electromagnetic signals on human glioblastoma cells and mouse fibroblast cell lines and detected no DNA damage in cells, including the 24-hour period (33,34). In a similar study, Tice et al demonstrated that 837 and 1909.8 MHz radiofrequency waves did not result in a significant DNA damage in leukocytes as a result of 3 and 24 hour exposures (35).

Atasoy et al. examined the effects of electromagnetic fields on peripheral mononuclear cells in-vitro. The primary objective of this study was to analyze the changes in the cell viability, rates of apoptosis, proliferation indices and cell surface antigenic structures resulting from 2-, 6- and 24-hour exposure of mononuclear cells isolated from the peripheral blood to 450, 900 and 1784 MHz electromagnetic waves. Data obtained showed that electromagnetic waves didn't have any effect on cell viability, rates of apoptosis and proliferation index.

| Author | Year | Studied subject | Frequencies | Results |
|--------------------------|------|--|-------------------------|---|
| Goodman et al. | 1983 | RNA transcription | Pulsed EMF | increased activity of mRNA |
| Takashi et al. | 1986 | DNA synthesis | 10-100 Hz | DNA synthesis is not repressed |
| Goodman and Henderson | 1988 | salivary gland cells | 1,5-72 Hz ELF | alters polypeptide synthesis |
| Maes et al. | 1997 | Peripheral blood cells and Mitomycin C | 935.2 MHz | combined exposure revealed weak effect |
| Malyapa RS et al. | 1997 | Human blastoma cells | 835,62 and 847,74 | No DNA damaged |
| Malyapa RS et al. | 1997 | cultured mammalian cells | continuous 2450 MHz | No DNA damaged |
| Brusick et al. | 1998 | Nucleic acids | 800-3000 mHz | Not directly mutagenic, predominantly hyperthermia |
| Vijayalaxmi et al | 2000 | Peripheral blood cells | pulsed 2450 mHz | No DNA damaged |
| Milani et al. | 2001 | human lymphocytes | EMF | deviation of metabolic activity |
| Tian et al. | 2002 | Apoptosis | ELF and X-Ray | suppress apoptosis |
| Zyrmec, Jerman, Lahajnar | 2002 | E. Coli ATP synthesis | 100 Hz, alternate | stimulate ATP synthesis |
| Tice et al. | 2002 | Leukocytes | 837 and 1909,8 MHz | No DNA damaged |
| Wolf et al. | 2005 | NfkB and cell destruction | 50 Hz, 0,5-1 mT ELF-EMF | influences cell proliferation and DNA damage |
| Giladi et al. | 2008 | Cell growth | 10 Mhz | IF arrests cell growth |
| Kirson ED et al. | 2009 | human carcinoma cell series | TT Fields + chemo | increase of chemo efficacy |
| Atasoy A et al. | 2009 | peripheral mononuclear cells | 450, 900, 1784 MHz | No effect cell viability, effect of functional capacity |
| Coskun S et al. | 2009 | plasma liver brain specimens of pigs | 50 Hz, 1,5 mT EMF | Intermittant EMF effective on plasma lipid peroxydation |
| Akan A et al. | 2010 | Monocyt derived macrophage | 50 Hz, 1 mT ELF-EMF | supressed caspase 9 activation |
| Martinez-Samano J et al. | 2010 | antioxidant system liver kidney and plasma | 60 Hz, 2,4 mT | Decreased SOD and GSH |

Table 3. Some investigations and their results about cellular effects on electromagnetic fields.

While electromagnetic waves didn't change HLADR and CD11b expression in the peripheral blood mononuclear cells, they decreased the CD11a expression and increased the CD49d expression. These data suggest that electromagnetic signals could affect the functional capacity of the peripheral blood mononuclear cells by changing their adhesion ability. Maybe these alterations are a sign of the immune system modulation (36).

Akan Z et al. evaluated the immune response of monocyte-derived macrophages to pathogens in extremely low frequency electromagnetic fields. In this study, human monocytic leukemia cell line were cultured and 1 mT EMF was applied for 4–6 h to cells induced with *Staphylococcus aureus* or interferon gamma/lipopolysaccharide (IF γ /LPS). Alterations in nitric oxide (NO), inducible nitric oxide synthase (iNOS) levels, heat shock protein 70 levels (hsp70), cGMP levels, caspase-9 activation, and the growth rate of *S. aureus* were determined. The growth curve of exposed bacteria was found to be lower than the control. Field application increased NO levels, and this increase was more prominent for *S. aureus*-induced cells and appeared earlier than the increase in cells without field application. A slight decrease was observed in iNOS levels whereas there was an increase in cGMP levels. A time-dependent increase was observed in hsp70 levels. When cells were induced with *S. aureus* or IF γ /LPS, field application produced higher levels of hsp70, and suppressed the caspase-9 activation. These data showed that ELF-EMF affect the response of immune system, which suggests that it can be considered for beneficial uses (37).

Another hypothesis of effects related with ELF-EMF is that it changes the free radical levels in the organism. Free radicals in the body are eliminated through two pathways. The first pathway is the non-enzymatic pathway including glutathione, vitamins, carotenoids and flavonoids, while the second pathway relies on the activity of the enzyme, which is the most effective pathway. The key enzymes include catalase and superoxide dismutase. ELF-EMF convert free radicals into less active molecules and eliminate them (38,39). There is a balance between production and elimination of free radicals. An imbalance can promote oxidative stress, eventually resulting in cell destruction. One of the markers indicating destruction is malondialdehyde, the end product of lipid peroxidation (40). Coskun et al. exposed guinea pigs to 50 Hz, 1.5 mT ELF-EMF for 4 days. And, they found that it increases malondialdehyde, nitric oxide and myeloperoxidase activity, and decreased Glutathion S transferase levels (41).

Martinez et al. evaluated the effects of exposure to ELF-EMF on the antioxidant systems in liver, kidney and plasma in Wistar rats. They found that two hours of 60 Hz EMF exposure led to early changes in free radical levels, and superoxide dismutase (SOD) activity in plasma and glutathione (GSH) content in heart and kidney were decreased, but there was no change in the lipid peroxidation (42).

4.2 Heavy metals exposure and electromagnetic hypersensitivity

Some people are more susceptible to exposure with electromagnetic fields from others. It is referred as Electrohypersensitivity (EHS). The pathophysiology of EHS is unknown. Some authors claimed it is concerned with heavy metal exposure. Heavy metals bound the proteins within tissues and organs are thought to have low toxicity. Mortazavi and co-workers have found that static magnetic field as well as microwave radiation emitted from mobile phones may induced the mercury vapor release from dental amalgam, increasing concentration of dissolved mercury in saliva among amalgam bearers (43,44,45).

4.3 Electromagnetic fields and blood-brain barrier

The blood-brain barrier (BBB) in mammals is composed of endothelial cells with tight junctions including pericytes and extracellular matrix. Transmembrane proteins form a physical barrier (43). BBB tightness is provided by the connective tissue cells called pericytes and the extracellular matrix of the basement membrane (44). These cells, extracellular components and surrounding neurons are all called 'neurovascular unit' (45). BBB is not available in certain regions of the brain, which include the median eminence, the area postrema and nucleus tractus solitarius in the brain stem, the posterior pituitary, subfornical organ in the hypothalamus, organum vasculosum, subcommissural organ and pineal gland (45).

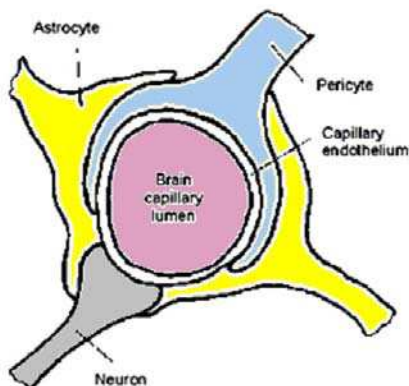


Fig. 2. Scheme of the blood brain Barrier.

4.3.2 Physiology of the blood-brain barrier

BBB allows for a more restricted Exchange of cells and molecules between the blood and the brain parenchyma. Transcellular and paracellular transport can occur not only via the blood vessel wall, but also via cranial and spinal nerve roots (46). Lipophilic compounds have unrestricted Access to the brain by passive diffusion through the endothelial cell membranes. Charged and hydrophilic molecules which are essential for brain metabolism, such as ions, amino acids, glucose and nucleic acid constituents pass the BBB through specialised channels or carriers. Water molecules can pass the BBB through protein channels called aquaporins or carriers (47). The transport of hydrophilic molecules such as proteins and peptides that do not have a specific transport system (48,49).

4.3.3 Thermal effects of EMF exposure on permeability

Environmental heat in excess of the mammalian thermoregulatory capacity can increase the permeability of the BBB to macromolecules (50). Neuronal albumin uptake in various brain regions was shown to be dose dependently related to brain temperature, with effects becoming apparent with temperature increases of 1 ° C or more (51). Thus, albumin bounded drugs uptake increases (52,53). In the study by Moriyama et al exposure of the Sprague-dawley rats head at microwave frequencies (at 2,5-3,2 GHz) that leads to a brain temperature above 40 ° C can increase BBB permeability (54). The degree of increased permeability depend on the degree of temperature rise and hence on the SAR of RF energy, on exposure duration and on the rate of heat distribution. Quock and co-workers assessed

permeability of capillary endothel cells after 2.45 GHz microwave irradiation cerebral cortex in albino rats (55). Quock and co-workers also demonstrated some hydrophilic drugs such as acetylcholine antagonist methylatropine, dopamin antagonist domperidone, and the chemotherapeutic drug methotrexate uptake can be increased with microwave induced hyperthermia (55,56).

Exposure to microwaves at thermal levels may make the brain more vulnerable for infections. Following microwave exposure at 2.5 GHz with SAR between 24-98 W/kg, increased BBB permeability to Horse radish proteins (HRP) was accompanied by increased lethality of japanase encephalitis virus (57).

4.4 Effects on nervous system and psychologic disorders

Due to mobile phones used close the brain tissue, electromagnetic waves affects it the most. Numerous studies have investigated the effect of exposure to radiofrequency electromagnetic waves from the mobile phone base stations on nervous system and behaviours (58). Rössli and co-workers conducted a systematic review of these studies, analysing 17 reports. Five of them were randomized human laboratory trials, and 12 were epidemiological studies. Most of these reports evaluated non-specific disease symptoms. Most of these studies investigated if there was an association between mobile phone base station (MPBS) radiation and development of acute symptoms during or shortly after exposure, and none of them found such an association. Consequently, based on these randomized, blinded, human laboratory trials, it can be concluded that there is good evidence for non-association between MPBS exposure up to 10 volt and development of symptoms. However, no sufficient data is available to draw conclusions about health effects of long-term low level exposure, which occurs in daily environment (9).

Ntzouni MP et al. investigated the effect of mobile phone radiation on short-term memory in mice. They evaluated the effects of mobile phone electromagnetic fields on non-spatial memory task (Object Recognition Task- ORT) that requires entorhinal cortex function. They applied the task to three groups of mice *Mus musculus* C57BL/6 (exposed, sham-exposed and control) combined with 3 different radiation exposure protocols. In the first protocol of acute exposure, mice 45 days old (postnatal day 45) were exposed to mobile phone radiation (SAR value 0.22W/kg) during the habituation, the training and the ORT test sessions (except the 10 minute inter-trial interval (ITI) with consolidation of stored object information). In the second protocol of chronic exposure-I, the same mice were exposed for 17 days for 90 minutes per day starting at post-natal day 55 to the same MP radiation. ORT recognition memory was only present during the ITI phase, and it was performed at post natal day 72 with radiation. In the third protocol of chronic exposure-II, mice received daily radiation under the same conditions for 31 days up to post natal day 86. On a day later, the ORT test was performed without any irradiation. A major effect was observed on the chronic exposure-I by the ORT-derived discrimination indices in three exposure protocols. It suggests a possible serious interaction between EMF and consolidation phase of the recognition memory processes. This may imply that the primary EMF target may be the information transfer pathway connecting the entorhinal-parahippocampal regions which participate in the ORT memory task (59).

A study by Heinrich S et al. has led to increasing concerns on the fact that increased number of mobile phone users, exposure to radiofrequency electromagnetic fields (RF EMF) may have potential adverse effects on acute health, particularly in children and adolescents. The authors assessed this potential relationship using personal dosimeters (60).

This population-based cross-sectional study conducted in Germany between 2006 and 2008, a 24-hour exposure profile was generated in 1484 children and 1508 adolescents. Personal interview data on socio-demographic characteristics, self-reported exposure and potential confounders were collected. Acute symptoms were evaluated twice during the study day using a symptom diary. Only a limited part of many associations assessed were found to be statistically significant. During noon time, adolescents with a measured exposure in the highest quartile during morning hours reported a statistically significant higher intensity of headache. During bedtime, adolescents with a measured exposure in the highest quartile during afternoon hours reported a statistically significant higher intensity of irritation in the evening while children reported a statistically significant higher intensity of concentration problems.

A limited number of statistically significant results, which were not consistent along the two time points, were observed. Furthermore, they couldn't confirm the significant results of the main analysis when 10% of the participants with the highest exposure. Based on the pattern of these results, they assumed that the few observed significant associations were not causal, but rather occurred by chance (60).

Sauter C et al. studied the potential effects of long-term exposure to Global System for Mobile Communications (GSM) 900 and Wideband Code Division Multiple Access (WCDMA) signals on attention and working memory. The results of studies showed the potential effects of electromagnetic waves emitted by mobile phones on cognitive functions are controversial. The sample consisted of 30 healthy male subjects, who were exposed to three exposure conditions in a randomly assigned and balanced order for nine days. All test were performed twice a day within a fixed timeframe on each test day. Univariate comparisons showed changes only in one parameter in vigilance test, and one parameter in divided attention test when subjects were exposed to GSM 900 compared to sham. In the WCDMA exposure condition, one parameter in the vigilance and one in the test on divided attention were altered compared to sham. Performance in the selective attention test and the n-back task was not affected by GSM 900 or WCDMA exposure. Time-of-day effects were evident for the tests on divided, selective attention, and working memory. Following the correction for multiple tests, only time of day effects remained significant for two tests. The authors concluded that results of their study did not provide any evidence of an EMF effect on human cognition, but they emphasize the necessity of control for time of day (61).

Lowden et al. examined the quality of sleep following an exposure to mobile phone in people who have symptoms associated with mobile phone use. Various studies showed increased activity for certain frequency bands (10-12 Hz) and for visually scored parameters during sleep after exposure to radiofrequency electromagnetic waves. Furthermore, shortening of REM duration has been reported. They evaluated the effects of a double-blind radiofrequency exposure (884 MHz, GSM signaling standard including non-DTX and DTX mode, time-averaged 10 g psSAR of 1.4 W/kg) on self-evaluated sleepiness and objective EEG measures during sleep. Forty-eight subjects with a mean age 28 years first underwent a 3 hours of controlled exposure prior to sleep (7:30-10:30 PM; active or sham), followed by a full-night polysomnographic recording in a sleep laboratory. The results following exposure showed that time in stages 3 and 4 decreased by 9.5 minutes (12%) while time in stage 2 increased by 8.3 minutes (4%). The latency to Stage 3 sleep was also prolonged by 4.8 min after exposure. Power density analysis indicated an enhanced activation in the frequency ranges 0.5-1.5 and 5.75-10.5 Hz during the first 30 min of Stage 2 sleep and 7.5-11.75 Hz elevation within the first hour of Stage 2 sleep, and bands 4.75-8.25 Hz elevated during the

second hour of Stage 2 sleep. No pronounced power changes were observed in SWS or for the third hour of scored Stage 2 sleep. No differences were found between controls and subjects with prior complaints of mobile phone-related symptoms. The results confirm previous findings that RF exposure increased the EEG alpha range in the sleep EEG, and indicated moderate impairment of SWS. Furthermore, reported differences in sensitivity to mobile phone use were not reflected in sleep parameters (62).

Valentini et al. published a metaanalysis which systematically reviewed the psychomotor effects of mobile phone electromagnetic fields. The authors indicate that during the last decade there has been increasing concern about the possible behavioral effects. This systematic review and meta-analysis focused on studies published since 1999 on the human cognitive and performance effects of mobile phone-related electromagnetic fields (EMF) with a search in the professional database of Pubmed, Biomed, Medline, Biological Sciences, Psychinfo, Psycarticles, Environmental Sciences and Pollution Management, Neurosciences Abstracts and Web of Sciences, and selection of 24 studies for metaanalysis. Each study had at least one psychomotor measurement result. Data were analysed using standardised mean difference (SMD) for measuring the effect size. Only three tasks (2-back, 3-back and simple reaction time (SRT)) displayed significant heterogeneity, but it didn't reach to a statistical significance. They concluded that mobile phone-like EMF did not seem to induce cognitive and psychomotor effects, and effects following chronic exposures should also be assessed (63).

Mohler et al. investigated the effect of every day radio frequency electromagnetic field exposure on sleep quality in a cross-sectional study. They assessed sleep disturbances and daytime sleepiness in a randomly selected population of 1375 subjects in Basel, Switzerland. They didn't observe any relationship between RF EMF exposure and sleep disturbances or excessive daytime sleepiness (64).

4.5 Effects on osteogenesis and chondrogenesis

Although extremely low electromagnetic fields have been shown to exert beneficial effects on cartilage tissue (65,66), Lin and Lin investigated the effect of pulsed EMF exposure on osteoblast cells, associated with decreased proliferation and mineralization (67). Okudan, Suslu and co-workers reported the influences of 50 Hz and 0 Hz (static) electric fields (EF), on intact rat bones, as evaluated by dual energy X-ray absorption (DEXA) measurements on bone content and density when the animals were continuously exposed in utero and neonatally to EFs. Differences between 50 Hz and control groups were found to be significant for total bone mineral density (BMD). Differences between static EF and control groups were also found to be significant for BMD. These results have shown that both static and 50 Hz EFs influence the early development of rat bones. However, the influence of static EFs is more pronounced than that of the 50 Hz field (68).

4.6 Effects on testis and spermatogenesis

Due to carrying mobile phones in the pockets, exposure of EMF on reproduction system has been growing interested. Tenorio showed in wistar rats, there were no change plasma testosterone levels but histopathological analyses showed testicular degeneration after the 30 minutes a day 60 Hz and 1 mT EMF exposure (69). In contrast, Ozguner and co-workers showed 900 MHz EMF exposure for rats, lends no support to suggestions of adverse effect on spermatogenesis, and on germinal epithelium. But there was a significant decrease in serum total testosterone level, and plasma LH and FSH levels in EMF group ($p < 0.05$) (70).

4.7 Carcinogenesis and electromagnetic waves

Since the first observation by Wertheimer and Leeper in 1979, a lot of epidemiologic investigations done between magnetic fields exposure and cancer. Speculations that electromagnetic waves can be carcinogenic increased the number of relevant epidemiological and in vitro studies (71,72).

4.7.1 Lymphatic and hematopoietic cancers

Some epidemiological trials have published data stating that the exposure to high-frequency electromagnetic fields may be associated with lymphatic and hematopoietic cancer. A survey conducted in people living around the Vatican radio station reported more childhood leukemia cases than expected (73). Similar data were also obtained from another study performed by Hocking et al in Australia (74). Hocking et al reported a higher leukemia incidence among adults and children living 2 km around Television transmitter stations. However, in these studies, it is stated that a definite correlation can not be established due to the scarcity of leukemia cases and due to the fact that no measurements were performed in leukemia patients on exposure to radiofrequency waves. A study by Morgan et al conducted on 195 775 subjects working in units related to wireless device manufacturing, design and tests detected that mortality associated with brain cancer, leukemia and lymphoma is not higher in this population compared to the normal population (75). In a study performed in Denmark, the analysis of 450 085 mobile phone users revealed no increase in the brain cancer incidence (76).

Previous pooled analyses reported an association between magnetic fields and childhood leukemia. A pooled analysis was presented based on the primary data from studies on residential magnetic fields and childhood leukemia published after 2000. The analysis included 7 studies with a total of 10,865 cases and 12,853 controls. The main analysis focused on 24-hour magnetic field measurements or calculated fields in residences. In the combined results, risk increased with increase in exposure, but the estimates were imprecise. The odds ratios for exposure categories of 0.1-0.2 μT , 0.2-0.3 μT and ≥ 0.3 μT , compared with <0.1 μT , were 1.07 (95% CI 0.81-1.41), 1.16 (0.69-1.93) and 1.44 (0.88-2.36), respectively (77). With the exception of the most influential Brasil study, the odds ratio somewhat increased. Furthermore, a non-parametric analysis using a generalised additive model suggested an increasing trend (78).

According to Elliott et al., epidemiological evidences suggested that extremely low frequency magnetic field exposure with a chronic low intensity is associated with increased childhood leukemia. The causality of this association is uncertain. They conducted a national case control study regarding the relationship between average magnetic fields from high voltage overhead power lines in the address at birth and childhood cancer using the National Grid records (79).

Draper et al observed 28,968 children born in England and Wales between 1962 and 1995, and received a diagnosis under 15 years of age. They found that the estimated relative risk for each 0.2 μT increase in magnetic field was 1.14 (95% confidence interval 0.57 to 2.32) for leukaemia, 0.80 (0.43-1.51) for CNS/brain tumours, and 1.34 (0.84-2.15) for other cancers. Although not statistically significant, their estimate for childhood leukaemia was similar to the results of comparable studies. The estimated attributable risk was below one case per year. They concluded that magnetic-field exposure during the year of birth was unlikely to be the whole cause of the association with distance from overhead power lines as previously reported (80).

| Authors | Brain tumours | | Brain tumors short latency | | Brain tumors longer latency | |
|---|--|--|--|---|---|--|
| | No. exp cases | RR estimate (95% CI) | No. exp cases | RR estimate (95% CI) | No. exp cases | RR estimate (95% CI) |
| Hardell et al. 1999 | 78 | 1.0 (0.7-1.4) | 78 | 1.0 (0.7-1.4) >1 yr | 34 16 | 0.8 (0.5-1.4) >5 yr 1.2 (0.6-2.6) >10 yr |
| Muscat et al. 2000 | 66 | 0.8 (0.6-1.2) | 28 | 1.1 (0.6-2.0) 2-3 yr | 17 | 0.7 (0.4-1.4) >4 yr |
| Inskip et al. 2001 | 139 | 0.8 (0.6-1.1) | 51 | 1.0 (0.6-1.6) 0.5-3 yr | 54 22 | 1.0 (0.6-1.6) > 3 yr 0.7 (0.4-1.4) >5 yr |
| Johansen et al. 2001 | 154 | 1.0 (0.8-1.1) | 87 | 1.1 (0.9-1.3) 1-4 yr | 24 | 1.0 (0.7-1.6) >5 yr |
| Auvinen et al. 2002 | 40 analogue 16 digital | 1.3 (0.9-1.8) | 15 analogue 11 digital | 1.2 (0.7-2.0) 1-2 yr | 17 analogue 1 digital | 1.5 (0.9-2.5) >2 yr |
| Hardell et al. 2002 | 188 analogue 224 digital | 1.3 (1.0-1.6) 1.0(0.8-1.2) | 188 analogue 224 digital | 1.3 (1.0-1.6) >1 yr 1.0(0.8-1.2) >1 yr | 46 analogue 33 digital | 1.3 (0.8-2.3) >10 yr 0.9 (0.6-1.5) >5 yr |
| Lönn et al. 2005 | 214 glioma 118 meningioma | 0.8 (0.6-1.0) 0.7 (0.5-0.9) | 112 64 | 0.8 (0.6-1.1) 1-4 yr 0.6 (0.4-0.9) 1-4 yr | 25 12 | 0.9 (0.5-1.5) >10 yr 0.9 (0.4-1.9) >10 yr |
| Christensen et al. 2005 | 47 low-grade glioma 59 high-grade glioma 67 meningioma | 1.1 (0.6-2.0) 0.6 (0.4-0.9) 0.8 (0.5-1.3) | 19 24 35 | 0.9 (0.4-1.8) 1-4 yr 0.6 (0.3-1.0) 1-4 yr 0.8 (0.5-1.3) 1-4 yr | 6 8 6 | 1.6 (0.4-6.1) >10 yr 0.5 (0.2-1.3) >10 yr 1.0 (0.3-3.2) >10 yr |
| Hardell et al. 2005a, Hardell et al. 2005b | 68 malignant, analogue 198 malignant, digital 35 meningioma, analogue 151 meningioma, digital | 2.6 (1.5-4.3) 1.9 (1.3-2.7) 1.7 (1.0-3.0) 1.3 (0.9-1.9) | 20 analogue 100 digital 1 analogue 96 digital | 1.8 (0.9-3.5) 6-10 yr† 1.6 (1.1-2.4) 1-5 yr 1.2 (0.1-12) 1-5 yr 1.2 (0.8-1.8) 1-5 yr | 48 analogue 19 digital 20 analogue 8 digital | 3.5 (2.0-6.4) >10 yr 3.6 (1.7-7.5) >10 yr 2.1 (1.1-4.3) >10 yr 1.5 (0.6-3.9) >10 yr |
| Hepworth et al. 2006 | 508 glioma | 0.9 (0.8-1.1) | 271 glioma | 0.9 (0.7-1.1) 1.5-4yr | 170 glioma 66 glioma | 1.0 (0.8-1.3) 5-9 yr 0.9 (0.6-1.3) >10yr |
| Schüz et al. 2006 | 138 glioma 104 meningioma | 1.0 (0.7 - 1.3) 0.8 (0.6 - 1.1) | 82 glioma 73 meningioma | 0.9 (0.6 - 1.2) 1-4 yr 0.9 (0.6 - 1.2) 1-4 yr | 51 glioma 12 glioma 23 meningioma 5 meningioma | 1.1 (0.8-1.7) >5yr 2.2 (0.9-5.1) >10yr 0.9 (0.5-1.5) >5yr 1.1 (0.4-3.4) >10yr |

Table 4. Results of some epidemiological studies on mobile phone use and brain tumours. The table is modified from the report to the Swedish Radiation Protection board: Recent Research on EMF and Health Risks. Third annual report from SSI's Independent Expert Group on Electromagnetic Fields (SSI's Independent Group on Electromagnetic Fields 2005).

In a recent study by Cooke et al., they investigated if there was an increased risk of leukemia with mobile phone use. They evaluated a total of 806 leukemia cases with an age range of 18 to 59 years, who lived in southeastern England between 2003 and 2009 compared with 585 non-blood relatives as a control group. They found that mobile phone use for more than 15 years didn't statistically increase the risk for leukemia (81).

In conclusion, their results were consistent with the previous pooled analyses showing an association between magnetic fields and childhood leukemia. Generally, the association was weaker in the most recently conducted studies, but they were small and lack methodological improvements needed to resolve the apparent association. The authors concluded that recent studies on magnetic fields and childhood leukaemia did not alter the previous assessment that magnetic fields are possibly carcinogenic (79).

4.7.2 Brain tumors

Baldi I et al. indicate that the etiology of brain tumors mainly remains unknown, and among potential risk factors, electromagnetic field exposure is suspected. They analyzed the relationship between brain tumors and occupational or residential exposure in adults. They carried out a case control study in southwestern France between May 1999 and April 2001. The study included a total of 221 central nervous system tumors and 442 individually age- and sex-matched controls selected from the general population. Electromagnetic field exposure was assessed in occupational settings through expert judgement based on complete job calendar, and at home by assessing the distance to power lines with the help of a geographical information system. Confounders such as education, use of home pesticide, residency in a rural area and occupational exposure to chemicals were taken into account. Separate analyses were performed for gliomas, meningiomas and acoustic neurinomas. A nonsignificant increase in risk was found for occupational exposure to electromagnetic fields. It was found that the risk for meningioma was higher in subjects living in the vicinity of power lines when the increase was considered separately for ELF. These data suggested that occupational or residential exposure to ELF may play a role in the occurrence of meningioma (82).

The most recent review by Khurana et al. investigated the relationship of wireless phone use for more than 10 years with a risk of brain tumor. This review covering a total of 11 metaanalyses showed that the brain tumors, namely glioma and acoustic neuroma increased 2-fold in people using wireless phones for more than 10 years, achieving a statistical significance (83).

5. Conclusions

Although electronic devices and the development in communications makes the life easier, it may also involve negative effects. These negative effects are particularly important in the electromagnetic fields in the Radiofrequency (RF) zone which are used in communications, radio and television broadcasting, cellular networks and indoor wireless systems. Along with the widespread use of technological products in daily life, the biological effects of electromagnetic waves has began to be more widely discussed.

The general opinion is that there is no direct evidence of hazardous effects on human health incurred by low-frequency radiofrequency waves. Studies at the cellular level, which uses relatively higher frequencies, demonstrate undesirable effects. In recent years there are a lot

of studies about effects of EMF on cellular level; DNA, RNA molecules, some proteins, and hormones, intracellular free radicals, and ions are shown.

Particularly, the dramatically increasing number of mobile phones users rise significant concerns due to its potential damage on people exposed by radiofrequency waves. There are increasing number of *in vivo*, *in vitro*, and epidemiologic studies on the effects of mobile phones, base stations and other EMF sources in last decade.

Epidemiologic evidence compiled in the past ten years starts to indicate an increased risk, in particular for brain tumor, from mobile phone use. Because of mobile phones used close the brain tissue, electromagnetic waves affects it the most. The magnitude of the brain tumor risk is moderate.

A literature search on 'mobile phone use and cancer' in Pubmed lists 350 studies. More than half of all of these studies is related to brain tumors. At present, evidence for a causal relationship between mobile phone use and brain tumors relies predominantly on epidemiology, in particular on the large studies on this subject. However, the etiopathogenesis of this causal relationship is not clear. The absence of this clear etiology even raise doubts about the cause itself. Weak evidence in favor of a causal relationship is provided by some animal and *in vitro* studies, but overall, genotoxicity assays, both *in vivo* and *in vitro*, are inconclusive to date.

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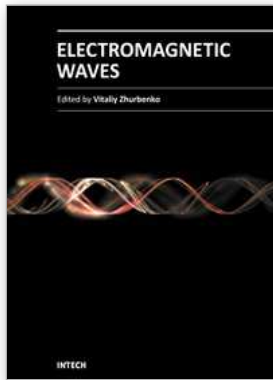
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