Data Centers Increase Electromagnetic Fields (EMF) Exposure

Large data centers require massive electrical infrastructure, including high-capacity substations, transformers, switchgear, and transmission corridors. The new and expanded electrical transmission line rights-of-ways have cut through neighborhoods, parks and conserved land.

These electrical systems generate extremely low frequency (ELF) electromagnetic fields (EMFs), particularly magnetic fields associated with high-voltage power lines as well as stray voltage and power quality distortion, including harmonics and high-frequency transients (EMI, dirty electricity) from large electrical loads, switching power supplies, and high-frequency power conversion equipment. As data center demand grows, so does the scale of the surrounding electrical infrastructure, likely increasing community exposure to EMFs.

Montgomery County Bill 4-26 should ensure a moratorium on data centers to address the numerous environmental issues from water and air pollution to EMF exposure. EMFs from the electrical grid build for data centers must be properly mitigated.

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Scientific Research on EMF and Health

Scientific research over several decades has examined health effects associated with long-term exposure to elevated ELF magnetic fields. Several epidemiological studies have reported associations between chronic residential exposure and increased risk of childhood leukemia.

Industry and international guidelines primarily address short-term, acute effects (such as nerve stimulation), and are set far above the levels associated with childhood cancer in long-term epidemiological studies. In 2002, the International Agency for Research on Cancer (IARC) determined that ELF-EMF magnetic fields are “possibly carcinogenic” to humans due to this research.

Although the US does not have federal safety limits, the often cited ICNIRP and IEEE exposure limits for 60 Hz fields \are 2,000–9,000 milligauss. However, the levels where epidemiologic studies have reported associations with childhood leukemia are 3–4 milligauss, thousands of times lower. People living in homes very close to powerlines can be exposed to 3-4 milligauss due to the proximity and it is perfectly legal. **No laws have been broken, yet no laws exist.**

As transmission corridors expand and electrical loads intensify near residential areas and schools, measures to mitigate exposure should be a part of the broader public health discussion.

Studies Have Found Increased Cancer

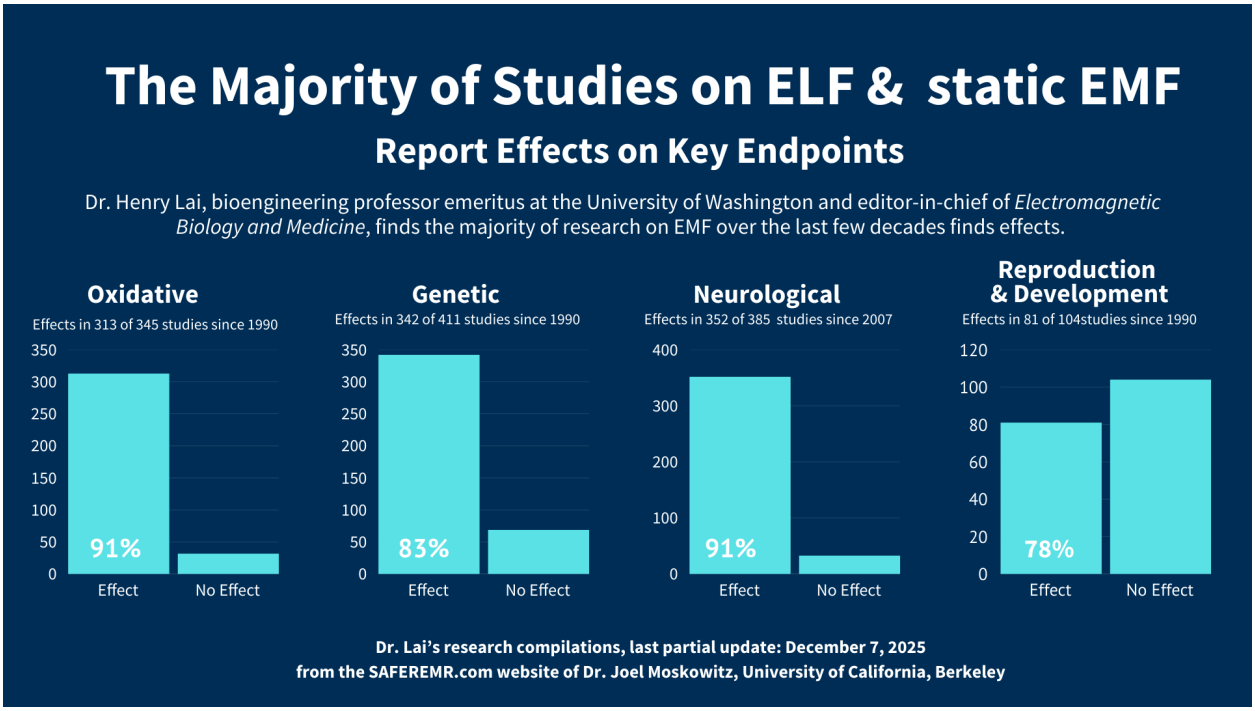
- A 2022 systematic review by Brabant et al. in Reviews on Environmental Health found that long-term exposure to magnetic fields above 0.4 μT (4 milligauss) was associated with increased risk of childhood leukemia, particularly acute lymphoblastic leukemia.
- A 2021 meta-analysis of 33 studies concluded a significant association between powerline ELF exposure and childhood leukemia, with possible dose-response effects.
- A study of children in Mexico City by Correa-Correa et al. 2025 found children exposed to 4 milligauss (ELF-EMF) in their homes had a significantly increased risk of central nervous system tumors.
- Kaiser Permanente studies reported that prenatal ELF-EMF exposure was associated with increased miscarriage risk and also ADHD, obesity, and asthma.

David Carpenter, MD, Director of the Institute for Health and the Environment at the University at Albany, published a review of the research showing that the source of funding affects study findings.

“The evidence that magnetic fields increase the risk of cancer is neither inconsistent nor inconclusive. Furthermore, adults are also at risk, not just children, and there is strong evidence for cancers in addition to leukemia, particularly brain and breast cancer.”

-David Carpenter in Environmental Research “Extremely low frequency electromagnetic fields and cancer: How source of funding affects results”

The Majority of Research Studies Find EMF Health Effects



Dr. Henry Lai, Professor Emeritus at the University of Washington, Editor Emeritus of the journal, Electromagnetic Biology and Medicine, and an emeritus member of the International Commission on the Biological Effects of EMF, has compiled summaries of the research on the biological effects of exposure to radio frequency (RFR) and extremely low frequency (ELF) and static electromagnetic fields (EMF). His set of abstracts, which covers the period from 1990 through November 2025 constitutes a comprehensive collection of the peer-reviewed research.

Dr. Lai reports that the preponderance of research has found that exposure to RFR or ELF EMF produces oxidative effects or free radicals, and damages DNA. This information is posted on Dr. Joel Moskowitz website SaferEMR.com.

Powerline EMF Linked to Alzheimer's Disease, and Cognitive Effects

Studies have found higher rates of Alzheimer's disease and other types of dementia close to high voltage powerlines.

A National Institute on Aging, National Institutes of Health supported study of high occupational ELF-EMF exposure reported associations with cognitive dysfunction and dementia, likely due to amyloid beta accumulation and reduced melatonin.

"The results of this study indicate that working in an occupation with high or M/H MF exposure may increase the risk of severe cognitive dysfunction. Smoking and older age may increase the deleterious effect of MF exposure."
-Davanipour et al in Journal of Advances in Medicine and Medical Research "Severe Cognitive Dysfunction and Occupational Extremely Low Frequency Magnetic Field Exposure among Elderly Mexican Americans"

As another example, a large 18-year nationwide cohort study published in Environment International (2026) found effects beginning around 0.5 mG (milligauss), with stronger associations observed in the 1–3 mG range, a range commonly found in homes close to electrical grid infrastructure.

The US never set federal safety standards on EMF

The US does not have federal safety limits for magnetic fields and electric fields. The exposure limits established by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) and the Institute of Electrical and Electronics Engineers (IEEE) are frequently cited in discussions of extremely low frequency (ELF) electromagnetic fields. However, these limits have important limitations when applied to environmental health, land-use planning, and long-term community exposure.

ICNIRP and IEEE ELF exposure limits are designed to prevent short-term, acute biological effects, such as nerve or muscle stimulation, and are not based on a risk assessment with robust review of scientific evidence related to long-term or lifetime exposure. ICNIRP and IEEE adopt a threshold-based approach focused on acute effects and are often misused as "proof of safety," which can obscure the need for risk mitigation.

ICNIRP and IEEE limits are set at levels far higher - thousands of times higher- than those associated with cancer and other adverse biological effects. The ICNRP and IEEE guidelines do not address proximity to homes or schools, duration of exposure, or opportunities to reduce exposure through design. In addition, they do not account for infrastructure-related factors such as grounding quality, neutral return paths, load variability, or stray currents, meaning compliance with the limits alone does not ensure good engineering practice or minimization of avoidable exposure.

The History of EPA Attempts to Set Limits for Powerline EMF

The U.S. once had a strong EPA research program, but it was defunded. Thus, the U.S. does not have a federal limit for exposure to ELF EMF or associated magnetic fields.

A major 2002 California State Health and Human Services report "An Evaluation of the Possible Risks From Electric and Magnetic Fields (EMFs) From Power Lines, Internal Wiring, Electrical Occupations and Appliances" concluded that EMFs may increase risks of childhood leukemia, brain cancer, ALS, and miscarriage. There have even been out-of-court settlements for EMF exposure, such as one in Massachusetts where high magnetic fields in a child's bedroom were linked to leukemia. However, in contrast to numerous other countries, the U.S. has no ongoing activities to create federal safety limits or ensure public health protection.

Other countries have more protections for EMF exposure in place

In contrast to the US. Numerous countries have policies to mitigate exposure to EMF hundreds and thousands of times lower

- The Netherlands: Since 2005, policies have been in place to reduce ELF-EMF in homes, schools, and kindergartens. In 2013, houses under 380–220 kV lines were bought out because of the ELF exposure. A 2018 Health Council report reaffirmed links to cancer and recommended reducing ELF-EMF.
- United Kingdom: Government promotes a precautionary policy to reduce EMF including optimum phasing for high-voltage overhead power lines, a series of engineering measures designed to reduce net currents, and encourages substations be sited away from homes. For low-voltage distribution networks (132 kV and below), the precautionary best practice measures to reduce EMF are set out in Engineering Recommendation G92 published by the Energy Networks Association.
- Germany: A 2013 Ordinance requires all feasible measures to minimize ELF-EMF exposure. 220 kV lines cannot be erected over buildings intended for long-term human occupancy.
- Israel: The maximum permissible ELF-EMF exposure in schools and residences is 4 mG per recommendations of the Ministry of Environment and the Ministry of Health.
- French Polynesia: The government-run public awareness campaign advises maintaining at least 1–1.5 meters from induction stoves and other EMF-generating appliances.
- France: Ministerial guidance discourages new hospitals, maternity wards, and childcare facilities near power lines, cables, and transformers where fields exceed 1 μT. The grid operator must monitor EMF emissions near power lines, and citizens can request measurements via local authorities.

- Slovenia: ELF limits are set at 10% of the EU reference value for new or modified installations near residences, schools, kindergartens, hospitals, playgrounds, parks, and public buildings.
- Denmark: Utilities must measure magnetic fields at new installations; annual averages should not exceed 4 mG, and no kindergartens or new buildings may be built near high-voltage lines.
- Switzerland: The Non-Ionizing Radiation Protection Act establishes precautionary EMF exposure limits for new installations.The country also measures, monitors and reports EMF levels.
- Croatia: Reduced ELF-EMF limits apply to sensitive areas, including homes, offices, schools, playgrounds, kindergartens, maternity wards, hospitals, and care facilities.
- Luxembourg: Ministerial recommendation prohibits new living spaces within 20 meters of 65 kV lines and 30 meters of 100–220 kV lines.
- Finland: The radiation authority STUK advises avoiding permanent residences where magnetic flux density continuously exceeds ~0.4 μT.
- Norway: A 0.4 μT "investigation level" applies to new homes, schools, kindergartens, and power lines; if exceeded, exposure-reduction measures are evaluated and implemented if reasonable.
- Italy: The 2017 Environment Ministry Decree recommends minimizing indoor ELF-EMF exposure; a precautionary "attention value" applies to 24-hour median exposure in homes, schools, playgrounds, and other spaces where people spend over 4 hours.
- Belgium: In Flanders, new power lines should be avoided near schools and childcare centers, and exposure over homes should be minimized. Year-averaged exposure near new schools and childcare centers should not exceed 4 mG. In Brussels, transformers near areas where children under 15 may be present must maintain a 24-hour average below 4 mG.

"4.1 Siting "DNOs should make reasonably practicable efforts not to site new final-distribution substations directly against living areas of homes etc (this is intended to cover homes, other residential properties, schools, libraries, and other public spaces with similar levels of occupancy)."

-From the United Kingdom- Guidelines for best practice in relation to electric and magnetic fields (EMFs) in the design and management of low voltage distribution networks, Engineering Recommendation G92 Issue 2 2018

Yet in the US, there are no policies to ensure people are protected. This must change.

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Review article

Extremely low frequency electromagnetic fields and cancer: How source of funding affects results

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ABSTRACT

While there has been evidence indicating that excessive exposure to magnetic fields from 50 to 60 Hz electricity increases risk of cancer, many argue that the evidence is inconsistent and inconclusive. This is particularly the case regarding magnetic field exposure and childhood leukemia. A major goal of this study is to examine how source of funding influences the reported results and conclusions. Several meta-analyses dating from about 2000 all report significant associations between exposure and risk of leukemia. By examining subsequent reports on childhood leukemia it is clear that almost all government or independent studies find either a statistically significant association between magnetic field exposure and childhood leukemia, or an elevated risk of at least OR = 1.5, while almost all industry supported studies fail to find any significant or even suggestive association. A secondary goal of this report is to examine the level of evidence for exposure and elevated risk of various adult cancers. Based on pooled or meta-analyses as well as subsequent peer-reviewed studies there is strong evidence that excessive exposure to magnetic fields increases risk of adult leukemia, male and female breast cancer and brain cancer. There is less convincing but suggestive evidence for elevations in several other cancer types. There is less clear evidence for bias based on source of funding in the adult cancer studies. There is also some evidence that both paternal and maternal prenatal exposure to magnetic fields results in an increased risk of leukemia and brain cancer in offspring.

When one allows for bias reflected in source of funding, the evidence that magnetic fields increase risk of cancer is neither inconsistent nor inconclusive. Furthermore adults are also at risk, not just children, and there is strong evidence for cancers in addition to leukemia, particularly brain and breast cancer.

1. Introduction

The first indication that extremely low frequency (ELF) electromagnetic fields (EMFs) coming from power lines and electricity could result in human disease was the report by Wertheimer and Leeper (1979) who found elevations in rates of childhood cancer in children living in homes in Denver, Colorado that were close to power lines which were presumed, based on a variety of considerations, to generate elevated magnetic fields within the home. While this conclusion was received skeptically, subsequent studies in several countries confirmed the observation. Four meta-analyses were published between 1998 and 2000 that concluded that there was a consistent and statistically significantly elevated risk of childhood leukemia in relation to residential proximity to elevated magnetic fields that could not be explained by random variation. Wartenberg (1998) considered 16 studies and reported an odds ratio (OR) of 1.44 (95%CL = 1.10–1.87) from studies that used indirect, wire-code analysis for exposure. Angelillo and Villari (1999) reported an OR = 1.46 (1.05–2.04) for six studies on wire code configuration and OR = 1.59 (1.14–2.22) for 4 studies with 24 h measured magnetic fields. Greenland et al. (2000) conducted their meta-analysis on 15 studies and found an OR = 1.52 (0.99–2.33) based on measured magnetic field for children living in homes with magnetic fields > 0.3 μT as compared to 0.1–0.2 μT, and 1.65 (1.15–2.35) based on wire code comparing children in homes with very high current code as compared to ordinary low current code. Ahlbom et al. (2000) performed a pooled analysis of results of nine studies that included 3203 children with leukemia as compared to 10,338 controls. They found an OR = 2.00 (1.27–3.13) for increased risk of leukemia in children with a residential magnetic field > 0.4 μT. Based primarily on the data included in these reviews the International Agency for Research on Cancer rated extra-low frequency electromagnetic fields (ELF-EMFs) as a Group 2b, possible human carcinogen (IARC , 2002).

In spite of this body of information, many have remained skeptical of the conclusion that exposure to power line magnetic fields really

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increases risk of childhood leukemia. There are several reasons for this, including the general problem that most animal exposure studies have not found increases in cancer, and uncertainty as to the mechanism(s) responsible. Comments are often made that there are a number of studies that do not report positive associations, and thus the conclusions are inconsistent. Therefore the question of whether or not magnetic fields associated with electricity pose hazards to human health has remained controversial. In addition to childhood leukemia, several other human diseases have been reported to be elevated among individuals with excessive exposure to magnetic fields. The goal of this review is to summarize the results of more recent investigations into the magnetic fields and childhood leukemia but also review associations with other cancers. In addition the source of funding of studies will be identified.

The question of whether or not magnetic field exposure causes cancer is extremely important, because in our modern world each of us is continuously exposed. Since there is no one that is unexposed studies must compare individuals with more vs. less exposure. While the risk estimates reported above are not particularly high, when the whole society is exposed to a carcinogen the implication for public health may be large.

2. Materials and methods

This review has been limited to those experimental studies of human cancer in relation to exposure to magnetic fields from power lines or other sources of electricity. Searches were done on pubmed and Google Scholar using the terms magnetic fields, ELF-EMF, power lines or electricity and cancer, leukemia, breast cancer, or brain cancer. For each cancer under consideration the results of recently published pooled or meta-analyses have been accepted and only more recently published additional peer-reviewed publications considered. For childhood leukemia search was for childhood leukemia studies after the meta-analyses published by Wartenberg (1998), Angelillo and Villari (1999), Ahlbom et al. (2000) and Greenland et al. (2000). For adult leukemia and brain cancer, studies were identified subsequent to the meta-analyses of Kheifets et al. (2008), for childhood brain cancer after the meta-analysis of Kheifets et al. (2010b). For male breast cancer studies were considered after the meta-analyses of Erren (2001) and Sun et el. (2013). For female breast cancer studies subsequent to Chen et al. (2013) and Zhao et al. (2014). Su et al. (2018) have published a meta-analysis specifically on parental occupational exposure to magnetic fields and risk of childhood central nervous system cancer. Zhang et al. (2016) published a meta-analysis of ELF-EMFs and all forms of cancer.

References were checked in several very recent reviews on magnetic fields to be sure that English-language, peer-reviewed publications were not missed. These include Kheifets et al. (2006, 2010a, b), Calvente et al. (2010), Zhao et al. (2014), Zhang et al. (2016) and Amoon et al. (2018).

3. Results

Table 1 shows results of peer-reviewed publications published since 2000 that report statistically significant associations between exposure to magnetic fields, either indirectly measured by wire code configuration, distance from the center of the power line (as magnetic fields decline to background over a distance of about 300 m) or directly measured, and childhood leukemia. The table includes numbers of cases and controls and the source of funding. Of these positive studies only one for which the funding source was identified was funded by an industry source.

Table 2 lists studies of childhood leukemia and magnetic field exposure that reported an elevated risk with an OR > 1.5, but for which the results are not statistically significant. All of these studies were funded by government agencies or private sources.

Table 3 lists studies of childhood leukemia and magnetic field exposure which do not show either a statistically significant association, nor have an OR greater than 1.5. All were primarily funded by industrial sources, although in some cases there was partial funding by governmental agencies.

There are three recent studies (Amoon et al., 2018; Crespi et al., 2019; Swanson et al., 2019), all supported by EPRI and National Grid, that have taken a new look at magnetic fields and childhood leukemia, and argue that neither distance from a power line nor measured magnetic fields alone predict risk. The authors acknowledge that there is "a small but consistent increased risk of childhood leukemia associated with exposures above 0.3 or 0.4 μT". Amoon et al. (2018) pooled results from 11 studies, and find a small but imprecise risk of childhood leukemia for residences < 50 m from 200 + KEV power lines, but argue that this result is not explained by high magnetic fields. The others argue that the risk values have been declining over time (Swanson et al., 2019) and, based on a model, that there is some other factor that is responsible for this elevated risk, not only magnetic field strength (Crespi et al., 2019). However they do not identify what other possible factor this might be.

In spite of these apparently discordant data, a recent meta-analysis of associations between measured magnetic fields and childhood leukemia show statistically significant associations (Zhou et al., 2014, government funded). In 11,699 case and 13,194 controls, they report an OR = 1.57 (1.03–2.40) when comparing exposures > 0.4 μT to < 0.1 μT, and OR = 2.43 (1.30–4.55) specifically for acute lymphocytic leukemia. When comparing exposures > 04 μT to < 0.2 μT they find OR = 1.31 (1.06–1.61).

4. Childhood brain cancer

Kheifets et al. (2010b) performed a utility-funded pooled analysis of ELF-EMFs and childhood brain cancer in relation to measured magnetic fields. In relation to 0.1–0.2 μT, those exposed to > 0.4 μT showed an OR = 1.14 (0.61–2.13). Other more recent reports were not found.

5. Adult cancers

The first publication reporting elevated rates of adult cancer in relation to magnetic field exposure was also by Wertheimer and Leeper (1982). They used a wire code to determine magnetic field exposure from neighborhood distribution lines but did not directly measure the magnetic fields: The wire code evaluated how close the line was to the home, how many wires were present, how thick the wires were (thicker wires indicating higher current flow) and how far the home was along the distribution system. The distance from the substation is important because the current flowing through the line decreases as it feeds other residences along the line. They determined wire code assignments into five categories of increasing magnetic fields in the homes of individuals who died from cancer as well as age , sex- and year of death-matched controls. They excluded most cases of lung cancer. They studied five different communities near to Denver, Colorado, and determined the ratio of cancer cases to controls. When comparing the highest to lowest surrogate of magnetic field exposure, the values varied between 121 and 164. (Using this method the value would be 100 if the rates were the same, would be greater than 100 if higher magnetic field posed a risk and less than 100 if magnetic fields were protective). There were statistically significant elevations for brain cancer, lymphoma, cancer of the uterus and breast, as well as non-significantly elevated cancers of the pancreas, bladder, kidney and prostate.

These results showing elevations in rates of several different types of cancer have been confirmed in more recent studies. Hakansson et al. (2002; government funded) investigated cancer in workers exposed to high levels of magnetic fields in industries using resistance welding in Sweden between 1985 and 1994. They studied 537,692 men and 180,529 women, and separated them into groups of low, medium, high and very high exposure based on their job title. Men in the high exposure category had increased incidence of kidney, pituitary gland and liver and biliary cancers, and the rates of these cancers increased with increased exposure. Women in the high exposure group had increased incidence of astrocytoma groups I-IV, and there was a clear exposure-response pattern. There were suggestions of an increase in uterine cancer and multiple myeloma, but these results were not statistically

Table 1
Studies reporting statistically significant positive associations between exposure to 50 or 60 Hz magnetic fields and childhood leukemia, and source of funding.

Authors	Type of measure	Level of Association	Funding
Schuz et al. (2001)	Measured (> 0.2 μT;		
	24 h	OR = 1.55 (0.65–3.67)	Government
	Night only	OR = 3.21 (1.33–7.80)	
	514 cases, 1301 controls		
Draper et al. (2005)	Distance (< 200 m)	RR = 1.69 (1 13-2.53)	Government
	Distance (< 600 m)	RR = 1.23 (1.02–1.49)	
	29081 cases of cancer, 9700 with leukemia, matched controls		
Kabuto et al. (2006)	Measured (> 4 μT)	OR = 4.67 (1.15–19.0)	Government
	312 ALL cases, 603 controls		
Mejia-Arangure et al., 2007 [a]	Measured (> 6 mG)	OR = 3.7 (1.05–13.1)	Government
	42 cases, 124 controls		
Lowenthal et al. (2007)	Distance (< 300 m for ages 0–15 years)		
		OR = 3.23 (1.26–8.29)	Private Foundations
	854 cases lympho- or myeloproliferative diseases, matched controls		
Svendsen et al., 2007 (Survival)	Measured		
	> 0.1 re < 0.2 μT	OR = 2.8 (1.2–6.2)	Government
	> 0.1 re > 0.2 μT	OR = 3.0 (0.9 = 9.8)	
	595 ALL cases		
Schuz et al. (2007)	Measured nighttime		EPRI
	0.1- < 0.2 μT	OR = 1.11 (0.91–1.36)	
	0.2 - < 0.4 μT	OR – 1.37 (0.99–1.90)	
	> 0.4 μT	OR = 1.93 (1.11–3.35)	
	1842 cases, 3099 controls		
Feizi and Arabi (2007)	Calculated (> 0.45 μT)	OR = 3.60, 1.11–12.39)	Not identified
	(70 cases, 69 controls)		
Rahman et al., 2008			Not identified
	Distance (< 200 m to > 200m)	OR = 2.30 (1.1–4.49)	
	(128 cases, 128 controls)		
Yang et al. (2008) [b]	Distance (< 50 m)	OR = 4.39 (1.43–13.54)	Government
	Distance (< 100 m)	OR = 4.31 (1.54–12.08)	
Sohrabi et al. (2010)	Distance (< 600 m) (300 cases, 300 controls)	OR = 2.61 (1.73–3.94)	Not identifiedGov
Tabrizi and Bidgoli, 2015	22 ALL cases 100 controls, prenatal and postnatal to power lines	OR = 3.6 (1.6-7.8)	

EPRI = Electric Power Research Institute.
ALL = Acute lymphocytic leukemia.
[a] Study of children with Down's Syndrome.
[b] Study of children with polymorphorisms of DNA repair genes.

significant. Zhang et al. (2016) performed a government-funded meta-analysis of all forms of cancer in association with ELF exposure. They reported on 42 studies with 13,259 cases, 100,882 controls, and found an overall OR = 1.08 (1.01–1.15). The strongest associations were for breast cancer and leukemia, and studies done in North America were more consistently positive than those from Europe.

6. Adult leukemia

There is a considerable body of evidence specifically on adult leukemia in relation to magnetic field exposure, a focus triggered by the studies of childhood leukemia. Feychting et al. (1997; government funded) studied adult leukemia in relation to both residential and occupational exposures. While neither alone showed significant results, when both sources of exposure were considered there was a significantly elevated risk of adult leukemia (OR = 3.7; 1.5–9.4). In a meta-analysis of data published up through 1997, Kheifets et al. (1997) concluded that most studies showed a small overall increase in risk [risk ratio (RR) = 1.18; 1.12–1.24]. Lowenthal et al. (2007) reported that children living within 300 m of a power line had an elevated (but not statistically significant) risk of developing leukemia (OR = 4.74; 0.98–22.9), while adults living within the same distance showed a smaller but significantly elevated risk (OR = 3.23; 1.26–8.29) (funded by private foundation).

Table 2
Studies showing non-significant elevations in risk with OR > 1.5.

Mizoue et al. (2004)	Distance (< 300 m)	OR = 2.2 (0.5–9.0)	Government
	Lived there long	OR = 3.4 (0.9–13.2)	
Malagoli et al. (2010)	Calculated > 0.1 μT from HVPL	OR = 3.2 (0.4–23.4)	Government
	64 cases, 64 controls		
Wuunsch-Filho et al., 2011	Measured (> 0.3 μT)	OR = 1.09 (0.33–3.61)	Government
	Distance (< 50 m)	OR = 3.57 (0.41–31.44)	
	Distance (< 200 m)	OR = 1.67 (0.49–5.75)	
Sermage-Faure et al. (2013)	ALL, HVPLs in France 2779 cases, 30,000 controls.	OR = 1.7 (0.9–3.6)	Gov/Private
	Distance (< 50 M of 225–400 KEV)		
	Distance (< 50 m of 63–150 KEV)	OR = 1.0 (0.6–1.7)	
Salvan et al. (2015)	409 cases, 569 controls Measured relative to < 0.1 μT		
	0.1–0.2 μT	OR = 1.87 (0,53-1.25)	Government
	> 0.2 μT	OR = 2.24 (1.03–4.88)	
	> 3 μT	OR = 0.75 (0.38–1.50)	

HVPL = high voltage power line.
KEV = killivolts

Table 3
Negative studies of magnetic or electric field exposures and childhood leukemia and source of funding.

UK Childhood Cancer, 2002	Measured (> 20 V/m cf to < 10 V/m) 273 cases, 276 controls	OR = 1.32 (0.73–2.39) All leukemia	Power Comp and private.
Foliart et al. (2007)	Measured 386 cases	No trend observed	EPRI/EDF
Kroll et al. (2010)	Modelled (each > 0.2 μT)	OR = 1.14 (0.57–2.32)	Gov/National Grid
Schuz et al. (2012) (Survival)	28,968 cases, 28,968 controls		
	Various (> 0.3 μT) 3074 cases	OR = 0.96 (0.49–1.89)	EPRI
Bunch et al. (2014)	Distance (< 200 m)	RR = 1.12 (0.90–1.38)	National Grid
	Distance (< 599 m)	RR = 0.99 (0.89–1.10)	
	53,515 cases of childhood cancer matched to at least one control		
Pedersen et al. (2014)	Distance (< 200 m)	OR = 0.76 (0.40–1.45)	Danish Energy
	Distance (< 599 m) 1698 cases, 3396 controls	OR = 0.92 (0.67–1.25)	and Private
Crespi et al. (2016)	Distance ((< 50 m) 5788 cases, 3308 controls	OR 1.4 (0.7–2.7)	EPRI and NCI

Kheifets et al. (2008) have done an extensive meta-analysis of 59 studies of ELF exposure and adult leukemia, including those reported earlier as well as those published since the 1997 report. When considering both the older and newer studies, the RR = 1.16 (1.11–1.22) for all leukemia. The strongest association was for chronic lymphocytic leukemia (CLL) (RR = 1.35; 1.10–1.65). This study was supported by EPRI.

There have been only a few studies since 2008 investigating adult leukemia and ELF exposure. Marcilio et al. (2011) reported on 1857 cases of leukemia and 4706 controls in a study funded by a utility. They report an RR = 1.47 (0.99–2.18) for residence within 50 m, and RR = 1.61 (0.91–2.86) for measured magnetic field > 3 mG. Huss et al. (2018) reported results from the Swiss national registry of 3.1 million death records using a job exposure matrix to different levels of ELF-EMFs as high, medium or low. They report a hazards ratio (HR) = 1.31 (1.02–1.67) for myeloid leukemias and HR = 1.26 (0.93–1.70) for acute myeloid leukemia. There was a non-significant elevation in HR for acute lymphocytic leukemia [HR = 1.21 (0.78–1.89)], chronic myeloid leukemia (CML) [HR = 1.20 (0.71–2.02)] and Hodgkin's lymphoma [HR = 1.27 (0.71–2.29)]. There was little evidence of associations with chronic lymphocytic leukemia, non-Hodgkin's lymphoma or multiple myeloma. Interestingly they also report a dose-dependent increase in lung cancer, although they suspect this is secondary to smoking, not ELF.

6.1. Adult brain cancer

There is also a significant body of evidence showing that exposure to excessive magnetic fields increases the risk of development of adult brain cancer. Kheifets et al. (1995) performed a meta-analysis of 29 reports of brain cancer. She found statistically significant elevations in the incidence of brain cancer among electrical engineers, welders, and power station workers, all of whom are routinely exposed to elevated magnetic fields.

Kheifets et al. (2008) performed a second meta-analysis of occupational ELF exposure and brain cancer in adults, funded by EPRI. On consideration of 47 studies they report an overall RR = 1.14 (1.07–1.22) for all brain cancers, and RR = 1.18 (1.1–1.26) for only glioma. In studies since that date, Coble et al. (2009) (government funded) reported finding no significant associations between job title classified based on expected magnetic field exposure, total years of exposure, cumulative lifetime exposure and average lifetime exposure for glioma (489 cases) or meningioma (197 cases) as compared to 799 controls. Baldi et al. (2011) in a government-funded study investigated adult brain cancer in France with measurement of both occupational exposure and residential distance from the power line. This is one of the few studies that found a higher odds ratio for meningioma [3.02 (1.10–8.26)] (84 cases and 174 controls) than glioma {1.20 (0.66–2.17)] (51 cases and 120 controls). There was no association between living within 100 m of power lines as compared to more than 100 m for glioma [OR = 0.66 (0.21–2.07)] but a non-significant elevated risk for meningioma [OR = 2.99 (0.86–19.40)]. Elliott et al. (2013) reported on adult brain cancer based on 6781 cases and 79,507 controls living or not living within 1000 m of a high-voltage power line, and found an OR = 1.22 (0.86–1.69)] (partial funding from utilities). Turner et al. (2014) (also partial funding from utilities) reported on adult primary glioma (1,939) and meningioma (1,822) from seven countries and based occupational exposure on a job matrix. They found no association with either cancer for life time exposure, but did report elevated associations for glioma [OR = 1.67 (1.36–2.07)] and meningioma [OR = 1.23 (0.97–1.57)] for exposures during the previous four years. They suggest that ELF may function as a promotor or stimulate progression of brain tumors. However Carlberg et al. (2018) (foundation funded) did not find any significant association between occupational exposure to magnetic fields and meningioma based on cumulative exposure, average exposure or maximum exposure.

A report by Carlberg et al. (2017) (foundation funded) drew a similar conclusion to that of Turner et al. (2014) with regard to recent EMF exposure. They studied life time occupational job matrix magnetic field exposure of 1346 glioma cases and 3485 controls, and results were analyzed relative to the grade of glioma. They found no significant association with cumulative μT-years or maximum exposed job, but an OR = 1.3 (1.003–1.6) (p for trend = 0.04) for occupational exposure where the average level was 0.27 μT or greater. For astrocytomas grades I to III (n = 363), there were no significant associations with cumulative exposure, average exposure or maximum exposure, but for astrocytoma grade IV (n = 687), commonly known as glioblastoma, there were significant associations with cumulative exposure of 8.52 μT years or more (0R = 1.5; 1.05–2.1) and average exposure of 0.27 μT or more (OR = 1.4; 1.03–2.0). However the significant associations were only for 1–4 years, 5–9 years and 10–14 years before diagnosis, with no significant association of 20 or more years. Thus these results are quite consistent with the conclusion that exposure in the recent past is important, as suggested by Turner et al. (2014). There was a significant p for trend between level of exposure and grade IV astrocytomas for years 1–14, but not for 15 or more years, and no significant association with all glioma in either 1–14 or 15 or more years. Their conclusion was that occupation exposure to ELF EMF serves as a promotion or progression factor, rather than as an initiator.

Hardell and colleagues have reported a number of studies showing an increased risk of gliomas and especially glioblastomas in individuals that have used mobile phone extensively (Hardell and Carlberg, 2009), and therefore they examined interactions between mobile phone use and ELF exposure on gliomas and astrocytomas grade IV. They did not find any interaction between ELF and mobile phone use for gliomas, indicating that they are independent risk factors. They conclude that radiofrequency EMFs are the major risk factor for gliomas.

6.2. ELF exposure and breast cancer

Erren (2001) reported a meta-analysis of ELF and female breast cancer from 24 studies, and found RR = 1.12 (1.09–1.15). Chen et al. (2010) reported a meta-analysis of 24,338 cases and 60,628 controls in 15 publications in relation to female breast cancer risk. They found no statistically significant associations (OR = 0.988; 0.898–1.088). However a different Chen et al. (2013)] also reported a meta-analysis of case-control studies published between 1990 and 2010 and found an OR = 1.07 (1.02–1.13) for 23 studies. Associations were positive for estrogen-positive and premenopausal breast cancer, but not for other forms. Zhao et al. (2014) have also published a meta-analysis of results of 16 studies published between 2000 and 2007 that reported on pre- and post-menopausal breast cancer. They find an OR = 1.10 (1.01–1.20) overall, and OR = 1.25 (0.93–1.18) for pre-menopausal women. There was no significant association for post-menopausal women. Zhang et al. (2016) also performed a meta-analysis of 23 studies of female breast cancer and reported an OR = 1.07 (1.00–1.15).

Erren (2001) reported a meta-analysis of 15 studies of male breast cancer in relation to ELFs, and found a RR = 1.37 (1.11–1.71). Sun et al. (2013) performed a meta-analysis of 18 studies of male breast cancer in relation to EMF exposures. This included seven case-control and 11 cohort studies. They report a pooled OR = 1.32 (1.14–1.52, $p < 0.001$). All of these breast cancer studies were funded by government agencies. Grundy et al. (2016) investigated occupational exposure to magnetic fields and male breast cancer in 115 cases and 570 controls. They classified magnetic field exposures into three categories based on job histories and duration. They found an elevated risk of breast cancer in men who were exposed to > 0.6 μT [OR = 1.80 (0.82–3.95)] as compared to men exposed to < 0.3 μT. In addition they found that men with any occupational exposure to magnetic fields for at least 30 years had an elevated risk of breast cancer [OR = 2.77 (0.98–7.82)] as compared to men with only background exposure.

6.3. Other cancers

There are also a few studies focused on other specific cancers. Baumgardt-Elms et al. (2002) found no elevated risk of testicular cancer in men who had ever worked near high voltage power lines [OR = 0.7 (0.38–1.18. Charles et al. (2003) reported an elevated risk of prostate cancer mortality in workers at US electric utility companies when comparing those with greater than 4.4 μT-years exposure as compared to those with < 0.6 μt years exposure (funded by EPRI and government). The author suggest that further study is needed on this association.

6.4. Parental ELF exposure and childhood cancer risk

There have been a number of studies of parental exposure to ELF-EMF and cancers in offspring. Feychting et al. (2000) followed 235,635 children from birth to14 years based on parent's job title. They did not find elevations in any childhood cancer based on mother's occupational exposure but did find a significant elevation in risk of leukemia (but not brain cancer) based on father's exposure [RR = 2.0 (1.1–3.5). By contrast Infante-Rivard and Deadman (2003) found an OR = 2.5 (1.2–5.0) for childhood leukemia based on mother's occupational exposure during pregnancy in a government-funded study. In a later study the same group performed a similar investigation of brain cancer in offspring of mothers' with ELF exposure estimated by a job title matrix and reported an OR = 1.5 (1.0–3.4) for astroglial tumors (Li et al., 2009). Among sewing machine operators, who are exposed to high magnetic fields, there was an OR = 2.3 (1.0–5.4) for all childhood brain tumors (government funded). Su et al. (2018) (government funded) performed a meta-analysis of 22 studies (21 case-control and one cohort study) of parental occupational exposure and childhood brain cancer. They report a strong association with maternal exposure [OR = 1.16 (1.06–1.26) and childhood brain cancer and a non-significantly elevated association with paternal exposure [OR = 1.15 (0.98–1.34)].

Pearce et al. (2007) reported on a population based registry of young people with cancer from Northern England, and examined risk of leukemia in offspring of men likely exposed to EMFs based on parental occupation on the child's birth records (funded by foundations). There was a significant elevation in childhood lymphoid leukemia in children whose fathers' occupation was as an electrician [OR = 1.59 (1.12–2.26). Hug et al. (2010) (government funded) studied German children's (ages 0 to 14) risk of developing cancer in relation to parents' pre-conceptual ELF exposure, based on occupation. They had 2382 controls and 2.049 cases, of which 846 were acute leukemia, 159 with non-Hodgkin's lymphoma, 444 with brain tumors and 600 with other solid tumors. They found no elevated risk in children whose fathers had occupational exposure to ELF-EMFs greater than 0.2 μT. Reid et al. (2011), in a government funded study, found no elevated risk of acute lymphocytic leukemia of either maternal [OR = 0.96 (0.74–1.25)] or paternal [OR = 0.78 (0.56–1.09)] occupational exposure. Auger et al. (2019) have reported on 784,944 Canadian newborns followed for one decade (government funded). There were 1114 children who developed cancer. They found a borderline elevated risk for development of any cancer [OR = 1.08 (0.98–1.20)], hematopoetic cancer [OT = 2.04 (0.88–1.23)] and solid tumors [OR = 1.11 (0.99–1.25)] for children living within 80 m of a transformer station as compared to > 200 m. However they did not find any association with living near to transmission lines.

7. Discussion

It is remarkable that in the 40 years after Wertheimer and Leeper (1979) first reported an association between exposure to magnetic fields from residential power lines and elevated risk of childhood cancer, and the large number of subsequent investigations, that there is still controversy over the question “Does exposure to magnetic fields cause cancer?” One contributing cause of the confusion is clear from the analysis of the source of funding. When childhood leukemia studies are funded by governments or private sources they consistently find that elevated exposure increases risk. When those studies are funded by utilities they consistently do not find positive associations. In some cases the same investigators find positive associations when funded by government and then go on to report negative finding when funded by utilities. The differences in findings cannot be explained by numbers of cases or other methodological factors, leading to the conclusion that conflicts of interest based on source of funding have influenced the results, whether this was due to conscious or unconscious design.

A similar finding of different results obtained based on funding source has been reported for use of mobile phones and brain cancer, where reports funded by the industry were least likely to find associations (Huss et al., 2007). Other have also commented on the degree to which ties to industry influences conclusions as to risks of cancer from EMF exposures, and how this goes beyond reports of original research to influences on national and international committees that issue summary reports (Hardell et al., 2006; Maisch, 2006; Starkey, 2016; Hardell, 2017). The overall result arising from these conflicts of interest is that the public is confused and many times the press declares that results are “inconsistent” when in fact they are very consistent if one does not consider the results of industry-funded studies.

While much of the debate as to whether magnetic fields increase the risk of cancer has focused on childhood leukemia, the evidence for an elevated risk for several adult cancers is strong and surprisingly consistent. While there remains a possibility of conflicts of interest here as well, it is not as apparent as in the case of childhood leukemia. But meta-analyses on magnetic field exposure and adult leukemia, brain cancer and breast cancer in both men and women are almost all positive. The data on parental exposure and childhood cancer is less strong and consistent, but there is sufficient indication that there may be an

association so as to merit additional study.

The specific mechanisms whereby exposure to magnetic fields increases risk of cancer are still uncertain, but we know that generation of reactive oxygen species and gene induction are involved (Belpomme et al., 2018). The recent animal studies from the Ramazzini Institute also provide additional insight, when considered in light of some of the human studies. Bua et al. (2018) did not detect any increase in cancer in Sprague-Dawley rats exposed to 50 Hz ELF-EMFs over their lifetime. However the same groups demonstrated that there was synergistic cancer promotion when magnetic fields were added to exposure to formaldehyde (Soffritti et al., 2016a) or an acute low-dose of ionizing radiation (Soffritti et al., 2016b). These results are consistent with the suggestion in the reports of Turner et al. (2014) and Carlberg et al. (2017) that magnetic fields function of promotors, not inducers, of cancer.

There are other implications of this analysis. We have accepted results of meta-analyses done by a number of different authors. However in none of these meta-analyses have industry-funded studies been excluded. If studies were included that were biased, the overall conclusions may have been underestimations of the true associations.

While the significant elevations in risk for the various forms of cancer are not large (significant ORs usually not much greater than 2), the reality is that everyone is exposed at various degrees, and therefore there is no unexposed population for comparison. This means that in each study one is comparing disease in individuals with more as compared to less exposure. This also will result in an underestimation of the true risk. The overall evidence presented above shows a clear increase in risk of various cancers associated with elevated field magnetic exposure, but these consideration lead to the conclusion that the actual risk is likely even greater than indicated by the meta-analyses because of bias in some reports as well as in the individual studies and because of the lack of an unexposed comparison population.

In spite of the evidence for there being an elevated risk of various cancers upon excessive exposure to magnetic fields, there has not been a general acceptance that such exposure is a hazard to human health of sufficient magnitude to merit doing anything about it. This represents a failure on the part of international and national institutions, as well as the medical and public health communities, and is in great part a consequence of the distortions promoted by those with clear conflicts of interest. But to have regulators, scientists and the public remain ignorant of the evidence of harm from excessive exposure is unacceptable. The concept of “prudent avoidance”, developed by Granger Morgan (1988) from Carnegie Mellon University some 30 years ago, remains invaluable. We are not going to reduce our use of electricity, but there are many simple ways to reduce excessive exposure to magnetic fields that do not interfere with the quality of life but will reduce the risk of developing cancer.

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Planetary electromagnetic pollution: it is time to assess its impact

As the Planetary Health Alliance moves forward after a productive second annual meeting, a discussion on the rapid global proliferation of artificial electromagnetic fields would now be apt. The most notable is the blanket of radiofrequency electromagnetic radiation, largely microwave radiation generated for wireless communication and surveillance technologies, as mounting scientific evidence suggests that prolonged exposure to radiofrequency electromagnetic radiation has serious biological and health effects. However, public exposure regulations in most countries continue to be based on the guidelines of the International Commission on Non-Ionizing Radiation Protection[1] and Institute of Electrical and Electronics Engineers,[2] which were established in the 1990s on the belief that only acute thermal effects are hazardous. Prevention of tissue heating by radiofrequency electromagnetic radiation is now proven to be ineffective in preventing biochemical and physiological interference. For example, acute non-thermal exposure has been shown to alter human brain metabolism by NIH scientists,[3] electrical activity in the brain,[4] and systemic immune responses.[5] Chronic exposure has been associated with increased oxidative stress and DNA damage[6,7] and cancer risk.[8] Laboratory studies, including large rodent studies by the US National Toxicology Program[9] and Ramazzini Institute of Italy,[10] confirm these biological and health effects in vivo. As we address the threats to human health from the changing environmental conditions due to human activity,[11] the increasing exposure to artificial electromagnetic radiation needs to be included in this discussion.

Due to the exponential increase in the use of wireless personal communication devices (eg, mobile or cordless phones and WiFi or Bluetooth-enabled devices) and the infrastructure facilitating them, levels of exposure to radiofrequency electromagnetic radiation around the 1 GHz frequency band, which is mostly used for modern wireless communications, have increased from extremely low natural levels by about 10^{18} times (figure). Radiofrequency electromagnetic radiation is also used for radar, security scanners, smart meters, and medical equipment (MRI, diathermy, and radiofrequency ablation). It is plausibly the most rapidly increasing anthropogenic environmental exposure since the mid-20th century, and levels will surge considerably again, as technologies like the Internet of Things and 5G add millions more radiofrequency transmitters around us.

Unprecedented human exposure to radiofrequency electromagnetic radiation from conception until death has been occurring in the past two decades. Evidence of its effects on the CNS, including altered neurodevelopment[14] and increased risk of some neurodegenerative diseases,[15] is a major concern considering the steady increase in their incidence. Evidence exists for an association between neurodevelopmental or

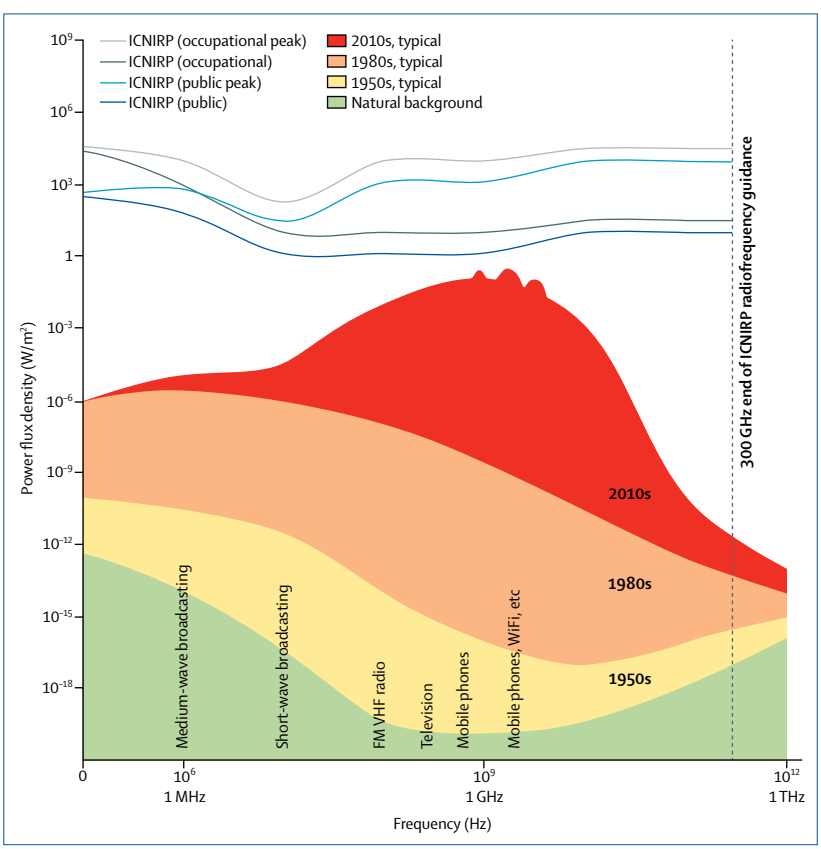

Figure: **Typical maximum daily exposure to radiofrequency electromagnetic radiation from man-made and natural power flux densities in comparison with International Commission on Non-Ionizing Radiation Protection safety guidelines[1]**

Anthropogenic radiofrequency electromagnetic radiation levels are illustrated for different periods in the evolution of wireless communication technologies. These exposure levels are frequently experienced daily by people using various wireless devices. The levels are instantaneous and not time-averaged over 6 minutes as specified by International Commission on Non-Ionizing Radiation Protection for thermal reasons. Figure modified from Philips and Lamburn[12] with permission. Natural levels of radiofrequency electromagnetic radiation were based on the NASA review report CR-166661.[13]

behavioural disorders in children and exposure to wireless devices,[14] and experimental evidence, such as the Yale finding, shows that prenatal exposure could cause structural and functional changes in the brain associated with ADHD-like behaviour.[16] These findings deserve urgent attention.

For the **Oceania Radiofrequency Scientific Advisory Association** see www.orsaa.org

At the Oceania Radiofrequency Scientific Advisory Association, an independent scientific organisation, volunteering scientists have constructed the world's largest categorised online database of peer-reviewed studies on radiofrequency electromagnetic radiation and other man-made electromagnetic fields of lower frequencies. A recent evaluation of 2266 studies (including in-vitro and in-vivo studies in human, animal, and plant experimental systems and population studies) found that most studies (n=1546, 68·2%) have demonstrated significant biological or health effects associated with exposure to anthropogenic electromagnetic fields. We have published our preliminary data on radiofrequency electromagnetic radiation, which shows that 89% (216 of 242) of experimental studies that investigated oxidative stress endpoints showed significant effects.[7] This weight of scientific evidence refutes the prominent claim that the deployment of wireless technologies poses no health risks at the currently permitted non-thermal radiofrequency exposure levels. Instead, the evidence supports the International EMF Scientist Appeal by 244 scientists from 41 countries who have published on the subject in peer-reviewed literature and collectively petitioned the WHO and the UN for immediate measures to reduce public exposure to artificial electromagnetic fields and radiation.

For the **International EMF Scientist Appeal** see www.emfscientist.org

Evidence also exists of the effects of radiofrequency electromagnetic radiation on flora and fauna. For example, the reported global reduction in bees and other insects is plausibly linked to the increased radiofrequency electromagnetic radiation in the environment.[17] Honeybees are among the species that use magnetoreception, which is sensitive to anthropogenic electromagnetic fields, for navigation.

Man-made electromagnetic fields range from extremely low frequency (associated with electricity supplies and electrical appliances) to low, medium, high, and extremely high frequency (mostly associated with wireless communication). The potential effects of these anthropogenic electromagnetic fields on natural electromagnetic fields, such as the Schumann Resonance that controls the weather and climate, have not been properly studied. Similarly, we do not adequately understand the effects of anthropogenic radiofrequency electromagnetic radiation on other natural and man-made atmospheric components or the ionosphere. It has been widely claimed that radiofrequency electromagnetic radiation, being non-ionising radiation, does not possess enough photon energy to cause DNA damage. This has now been proven wrong experimentally.[18,19] Radiofrequency electromagnetic radiation causes DNA damage apparently through oxidative stress,[7] similar to near-UV radiation, which was also long thought to be harmless.

At a time when environmental health scientists tackle serious global issues such as climate change and chemical toxicants in public health, there is an urgent need to address so-called electrosmog. A genuine evidence-based approach to the risk assessment and regulation of anthropogenic electromagnetic fields will help the health of us all, as well as that of our planetary home. Some government health authorities have recently taken steps to reduce public exposure to radiofrequency electromagnetic radiation by regulating use of wireless devices by children and recommending preferential use of wired communication devices in general, but this ought to be a coordinated international effort.

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Thermal and non-thermal health effects of low intensity non-ionizing radiation: An international perspective☆

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ABSTRACT

Exposure to low frequency and radiofrequency electromagnetic fields at low intensities poses a significant health hazard that has not been adequately addressed by national and international organizations such as the World Health Organization. There is strong evidence that excessive exposure to mobile phone-frequencies over long periods of time increases the risk of brain cancer both in humans and animals. The mechanism(s) responsible include induction of reactive oxygen species, gene expression alteration and DNA damage through both epigenetic and genetic processes. *In vivo* and *in vitro* studies demonstrate adverse effects on male and female reproduction, almost certainly due to generation of reactive oxygen species. There is increasing evidence the exposures can result in neurobehavioral decrements and that some individuals develop a syndrome of "electro-hypersensitivity" or "microwave illness", which is one of several syndromes commonly categorized as "idiopathic environmental intolerance". While the symptoms are non-specific, new biochemical indicators and imaging techniques allow diagnosis that excludes the symptoms as being only psychosomatic. Unfortunately standards set by most national and international bodies are not protective of human health. This is a particular concern in children, given the rapid expansion of use of wireless technologies, the greater susceptibility of the developing nervous system, the hyperconductivity of their brain tissue, the greater penetration of radiofrequency radiation relative to head size and their potential for a longer lifetime exposure.

1. Introduction

Electromagnetic fields (EMFs) are packets of energy that have no mass. They vary in frequency and wavelength. At the high end of the electromagnetic spectrum there are cosmic and X-rays that have enough energy to cause ionization, and therefore are known as ionizing EMFs. Below in frequency and energy are ultraviolet, visible light and infrared EMFs. Excessive exposure to ultraviolet EMFs poses clear danger to human health, but life on earth would not be possible without visible light and infrared EMFs. Below these forms of EMF are those used for communications (radiofrequency or RF-EMFs, 30 kHz-300 GHz) and those generated by electricity (extremely low-frequency or ELF-EMFs, 3 Hz-3 kHz). These EMFs do not have sufficient energy to directly cause ionization, and are therefore known as non-ionizing radiation. RF-EMFs at sufficient intensity cause tissue heating, which is the basis of operation of the microwave oven. However the question to be addressed here is human health effects secondary to exposures to non-ionizing EMFs at low intensities that do not cause measureable heating.

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In spite of a large body of evidence for human health hazards from non-ionizing EMFs at intensities that do not cause measureable tissue heating, summarized in an encyclopedic fashion in the Bioinitiative Report (www.bioinitiative.org), the World Health Organization (WHO) and governmental agencies in many countries have not taken steps to warn of the health hazards resulting from exposures to EMFs at low, non-thermal intensities, nor have they set exposure standards that are adequately health protective. In 2001 the International Agency for Research on Cancer (IARC, 2002), part of the WHO, declared ELF-EMFs to be "possibly carcinogenic to humans", and in 2011 they made a similar declaration for RF-EMFs (Baan et al., 2011; IARC, 2013). The classification of RF-EMFs as a "possible" human carcinogen was based primarily on evidence that long-term users of mobile phones held to the head resulted in an elevated risk of developing brain cancer. One major reason that the rating was not at "probable" or "known" was the lack of clear evidence from animal studies for exposure leading to cancer. The US National Toxicology Program has released preliminary results of a study of long term exposure of rats to cell phone radiation which resulted in a statistically significant increase in brain gliomas, the same cancer found in people after long-term cell phone use, and schwannomas, a tumor similar to the acoustic neuroma also seen after intensive mobile phone use (Wyde et al., 2016). Similar results in rats have been reported in an independent study at the Ramazzini Institute with exposures similar to those from a mobile phone base station (Falcioni et al., 2018). This evidence, in conjunction with the human studies, demonstrates conclusively that excessive exposure to RF-EMF results in an increased risk of cancer. In light of this new evidence for cancer in rodents in response to prolonged exposure to mobile phone frequencies, the IARC rating should be raised at least to "probable" (Group 2A) if not "known" (Group 1).

Unfortunately the International EMF Project of the WHO, which is part of the Department of Public Health, Environment and Social Determinants of Health in Geneva, has consistently minimized health concerns from non-ionizing EMFs at intensities that do not cause tissue heating (WHO, 2014). In this regard WHO has failed to provide an accurate and human health-protective analysis of the dangers posed to health, especially to the health of children, resulting from exposure to non-thermal levels of electromagnetic fields. The Department of Public Health, Environment and Social Determinates of Disease takes its advice on the issues related to human health effects of non-ionizing EMFs from the International Commission on Non-ionizing Radiation Protection (ICNIRP). Almost all members of the core group preparing the new Environmental Health Criteria (EHC) document for the WHO are members of ICNIRP (Starkey, 2016; Hardell, 2017), a non-goverment organization (NGO) whose members are appointed by other members. In spite of recent efforts to control for conflicts of interest, ICNIRP has a long record of close associations with industry (Maisch, 2006). When queried as to why the WHO would take recommendations from such a group, WHO staff replied that ICNIRP is an official NGO which works closely with the WHO. Why this should exclude other scientific research groups and public health professionals is unclear, particularly since most members of ICNIRP are not active researchers in this field. We are particularly concerned that a new WHO EHC document on RF-EMFs is scheduled to be released soon, and that the members of the EHC Core Group and the individuals whose assistance has been acknowledged are known to be in denial of serious non-thermal effects of RF-EMFs in spite of overwhelming scientific evidence to the contrary (Starkey, 2016; Hardell, 2017).

Others have dismissed the strong evidence for harm from ELF- and RF-EMFs by arguing that we do not know the mechanism whereby such low energetic EMFs might cause cancer and other diseases. We have definitive evidence that use of a mobile phone results in changes in brain metabolism (Volkow et al., 2011). We know that low-intensity ELF- and RF-EMFs generate reactive oxygen species (ROS), alter calcium metabolism and change gene expression through epigenetic mechanims, any of which may result in development of cancer and/or other diseases or physiological changes (see www.bioinitiative.org for many references). We do not know the mechanisms behind many known human carcinogens, dioxins and arsenic being two examples. Given the strength of the evidence for harm to humans it is imperative to reduce human exposure to EMFs. This is the essence of the "precautionary principle".

There are a number of reasons for our concern. In the past the major exposure of the general population to RF-EMFs came from radio and television signals. Now there are almost as many mobile phones as there are people in the world, all of them being exposed to RF-EMFs. There are mobile phone towers everywhere, and in many developing countries there are no land-lines that allow communication without exposure to RF-EMFs. There is rapid movement in many developed countries to place small cell transmitting devices (5G) operating at higher frequencies (24–70 GHz) every approximately 300 m along sidewalks in residential neighborhoods. There are other significant sources of exposure, coming from WiFi, smart meters and soon from automobiles operating without a human driver. Therefore human exposure has increased dramatically in recent years, and continues to increase rapidly. While we already are seeing harm from these exposures, the degree of harm will only increase with time because of the latency that is known to occur between exposure and development of diseases such as cancer.

Standards for protection of human health from EMFs vary greatly around the world. Many countries set standards based on the false assumption that there are no adverse health effects of RF-EMFs other than those that are caused by tissue heating. This is the case in North America, Australia and some European countries. Many countries from the former Soviet Union have much more restrictive standards. However information from cellular and human studies show biological effects that constitute hazards to human health at exposure levels that are often exceeded during daily life.

This report follows a recent non-official meeting in Geneva with WHO representives, where the authors urged WHO to acknowlege low intensity effects of ELF-EMFs and non-thermal health effects of RF-EMFs. This report does not attempt to present a complete overview of the subject [see the Bioinitiative Report (www.bioinitiative.org) for that] but rather to provide a holistic picture of the processes explaining most or all of the adverse effects of EMF exposures. It summarizes the evidence for cancer resulting from exposure to EMFs, and identifies other diseases or pathological conditions such as Alzheimer's disease and hypofertility that have been shown to be associated with excesive exposure to low-intensity EMFs. We also focus on electrohypersensitivity (EHS) in both children and adults and cognitive and behavioural problems in children resulting from the increasing exposure. Finally we discuss what is known about the mechanisms whereby non-thermal EMF radiation can cause disease with special reference to EMF-related free radical production and epigenetic and genetic mechanisms.

2. Mobile phone use and the risk for glioma, meningioma and acoustic neuroma

The brain is the main target for exposure to RF-EMF radiation during use of handheld wireless phones, both mobile and cordless phones (Cardis et al., 2008; Gandhi et al., 2012). An increased risk for brain tumors has been of concern for a long time. The results of the Swedish National Inpatient Register have documented an

increasing incidence of brain tumors in recent years (Carlberg and Hardell, 2017). In May 2011 RF radiation in the frequency range 30 kHz–300 GHz was evaluated to be a Group 2B, i.e. a "possible" human carcinogen, by IARC (Baan et al., 2011; IARC, 2013). This was based on an increased risk for glioma and acoustic neuroma in human epidemiological studies. In the following an updated summary is given of case-control studies on brain and head tumors; glioma, meningioma and acoustic neuroma. The Danish cohort study on 'mobile phone users' (Johansen et al., 2001; Schüz et al., 2006) is not included due to serious methodological shortcomings in the study design, including misclassification of exposure (see Söderqvist et al., 2012a).

2.1. Glioma

Glioma is the most common malignant brain tumor and represents about 60% of all central nervous system (CNS) tumors. Most of these are astrocytic tumors that can be divided into low-grade (WHO grades I-II) and high-grade (WHO grades III-IV). The most common glioma type is glioblastoma multiforme (WHO grade IV) with peak incidence in the age group 45–75 years and median survival less than one year (Ohgaki and Kleihues, 2005). Three research groups have provided results in case-control studies on glioma (Interphone, 2010; Coureau et al., 2014; Hardell and Carlberg, 2015). Hardell and colleagues have published results from case-control studies on use of wireless phones and brain tumor risk since the end of the 1990s (Hardell et al., 1990; for more discussion see Carlberg and Hardell, 2017).

A random effects model was used for meta-analyses of published studies, based on test for heterogeneity in the overall group ("all mobile"). Note that only the Hardell group also assessed use of cordless phones. Thus their reference category included cases and controls with no use of wireless phones in contrast to the other studies investigating only mobile phone use. In Table 1 results for highest cumulative use in hours of mobile phones is given. All studies reported statistically significant increased risk for glioma and the meta-analysis yielded an odds ratio (OR) = 1.90 [95% confidence interval (CI) = 1.31–2.76]. For ipsilateral mobile phone use the risk increased further to OR = 2.54 (95% CI = 1.83–3.52) in the meta-analysis based on 247 exposed cases and 202 controls.

Carlberg and Hardell (2014) found shorter survival in patients with glioblastoma multiforme associated with use of wireless phones compared with patients with no use. Interestingly mutation of the p53 gene involved in disease progression has been reported in glioblastoma multiforme in patients with mobile phone use ≥3 h per day. The mutation was statistically significantly correlated with shorter overall survival time (Akhavan-Sigari et al., 2014). Further support for the increased risk of glioma associated with mobile phone use has been obtained in additional analyses of parts of the Interphone study (Cardis et al., 2011; Grell et al., 2016; Momoli et al., 2017).

2.2. Meningioma

Meningioma is an encapsulated, well-demarked and rarely malignant tumor. It is the most common benign tumor and accounts for about 30% of intracranial neoplasms. It develops from the pia and arachnoid membranes that cover the CNS. It is slowly growing and gives neurological symptoms by compression of adjacent structures. The most common symptoms are headaches and seizures. The incidence is about two times higher in women than in men. Meningioma develops mostly among middle aged and older persons (Cea-Soriano et al., 2012). Carlberg and Hardell (2015) included meningioma in their case-control studies. The results of the meta-analysis for cumulative exposure in the highest category are given in Table 2. In total there was an increased (but not statistically significant) risk for cumulative exposure but the increased risk was statistically significant for ipsilateral use of mobile phones (OR = 1.49, 95% CI = 1.08–2.06).

2.3. Acoustic neuroma

Acoustic neuroma, also called vestibular schwannoma, is a benign tumor located on the eighth cranial nerve from the inner ear to the brain. It is usually encapsulated and grows in relation to the auditory and vestibular portions of the nerve. It grows slowly and due to the narrow anatomical space may give compression of vital brain stem structures. First symptoms of acoustic neuroma are usually tinnitus and hearing problems. Results for use of mobile phones in Interphone (2011) and Hardell et al. (2013) are given in Table 3. Statistically significant increased risk was found for cumulative ipsilateral use ≥1640 h yielding OR = 2.71 (95% CI = 1.72–4.28).

The study by Moon et al. (2014) was not included in the meta-analysis because data on cumulative mobile phone use with numbers of cases and controls were not given. Support of an increased risk was seen in the case-case part of the study (Moon et al., 2014) and also in the report by Sato et al. (2011). Pettersson et al. (2014) made a case-control study on acoustic neuroma in Sweden not overlapping the Hardell et al. (2013) study. An increased risk for the highest category of cumulative use of both mobile phone (≥680 h OR = 1.46, 95% CI = 0.98–2.17) and cordless phone (≥900 h OR = 1.67, 95% CI = 1.13–2.49) was found.Pettersson et al. (2014) was not included in the meta-analysis due to the many scientific shortcomings in the study, e.g. laterality analysis was not made for cordless phone, the numbers in the laterality analysis for mobile phone are not consistent in text and tables and the 'unexposed' reference category included subjects using either mobile and cordless phone, which is clearly not correct (Hardell and Carlberg, 2014).

Table 1
Numbers of exposed cases (Ca) and controls (Co) and odds ratio (OR) with 95% confidence interval (CI) for glioma in case-control studies in the highest category of cumulative hours of mobile phone use.

	All			Ipsilateral		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Interphone 2010						
Cumulative use ≥1640 h	210/154	1.40	1.03–1.89	100/62	1.96	1.22–3.16
Coureau et al., 2014						
Cumulative use ≥896 h	24/22	2.89	1.41–5.93	9/7	2.11	0.73–6.08
Carlberg and Hardell, 2015						
Cumulative use ≥1640 h	211/301	2.13	1.61–2.82	138/133	3.11	2.18–4.44
Meta-analysis						
Longest cumulative use	445/477	1.90	1.31–2.76	247/202	2.54	1.83–3.52

Table 2
Numbers of exposed cases (Ca) and controls (Co) and odds ratio (OR) with 95% confidence interval (CI) for meningioma in case-control studies in the highest category of cumulative hours of mobile phone use.

	All			Ipsilateral		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Interphone 2010						
Cumulative use ≥1640 h	130/107	1.15	0.81–1.62	46/35	1.45	0.80–2.61
Coureau et al., 2014						
Cumulative use ≥896 h	13/9	2.57	1.02–6.44	6/4	2.29	0.58–8.97
Carlberg and Hardell 2015						
Cumulative use ≥1640 h	141/301	1.24	0.93–1.66	67/133	1.46	0.98–2.17
Meta-analysis						
Longest cumulative use	284/417	1.27	0.98–1.66	119/172	1.49	1.08–2.06

Table 3
Numbers of exposed cases (Ca) and controls (Co) and odds ratio (OR) with 95% confidence interval (CI) for acoustic neuroma in case-control studies in the highest category of cumulative hours of mobile phone use.

	All			Ipsilateral		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Interphone 2011						
Cumulative use ≥1640 h	77/107	1.32	0.88–1.97	47/46	2.33	1.23–4.40
Hardell et al., 2013						
Cumulative use ≥1640 h	27/301	2.40	1.39–4.16	19/133	3.18	1.65–6.12
Meta-analysis						
Cumulative use ≥1640 h	104/408	1.73	0.96–3.09	66/179	2.71	1.72–4.28

2.4. In summary

Based on case-control studies there was a consistent finding of increased risk for glioma and acoustic neuroma associated with use of mobile phones. Similar results were found for cordless phones in the Hardell group studies, although such use was not reported by the other study groups. The findings are less consistent for meningioma although somewhat increased risk was seen in the meta-analysis of ipsilateral mobile phone use. A longer follow-up time is necessary for this type of slow growing tumor.

The results on glioma and acoustic neuroma are supported by results from animal studies showing co-carcinogenic and tumor promoting effects from RF-EMF (Tillmann et al., 2010; Lerchl et al., 2015). Recent results from the National Toxicology Program (NTP) study showed genotoxicity of RF radiation in rats and mice exposed to RF-EMF (Smith-Roe et al., 2017). That result supports previous findings of DNA strand breaks in rat brain cells exposed to RF-EMF (Lai and Singh, 1997).

Of importance also is that the results in the NTP and Ramazzini studies both demonstrated an increased incidence of tumors of the same type, glioma and malignant schwannoma, as has been seen in humans with mobile phone use (Wyde et al., 2016; Falcioni et al., 2018). Acoustic neuroma (vestibular schwannoma) is a similar type of tumor as malignant schwannoma, although benign. In fact, rates of brain tumors are increasing in Sweden and use of wireless phones has been suggested to be the cause (Hardell and Carlberg. 2017).

3. Other diseases and pathological conditions attributed to exposure to low-intensity EMFs

The evidence for harm from RF-EMF is strongest for cancer as a consequence of intensive mobile phone use, especially gliomas, glioblastomas and acoustic neuromas. But there is other evidence for elevation in risk of leukemia among children living near to very high intensity radio transmission towers (Michelozzi et al., 2002; Ha et al., 2007). This is particularly interesting because leukemia is the cancer most associated with elevated exposure to ELF-EMFs arising from power lines (Ahlbom et al., 2000; Greenland et al., 2000). There is some evidence for elevations in breast cancer risk among women who wear their mobile phones in their bra (West et al., 2013). Heavy use of a mobile phone was associated with significantly elevated rates of ipsilateral parotid tumors in studies from both Israel (Sadetzki et al., 2007) and China (Duan et al., 2011). No increased risk was found in a Swedish study, but the results were limited by low number of participants and lack of data on heavy and long-term use of wireless phones (Söderqvist et al., 2012b).

There are other significant human health hazards of concern. There is strong animal and human evidence that exposure to RF-EMFs as well as ELF-EMFs reduces fertility in both males (reviewed by McGill and Agarwal, 2014) and females (Roshangar et al., 2014). An association between spontaneous abortion and non-thermal EMF exposure including ELF-EMFs was reported in several case-control studies (Dodge, 1970; Juutilainen et al., 1993; Li et al., 2017). The increased use of mobile phones and increased exposure coming from WiFi, smart meters and other wireless devices has been paralled in time with male hypofertility and sperm abnormalities in semen (Rolland et al., 2013). These effects may be related to holding an active wireless laptop in a man's lap or having an active mobile phone on their belt, but more study is needed. There is evidence that isolated human sperm exposed to RF-EMFs are damaged by generation of reactive oxygen species (Agarwal et al., 2009).

There are other diseases or physiologic alterations which have been reported to be associated with exposure to non-thermal EMFs in humans and in animals (Belyaev et al., 2016). Alzheimer disease has been shown to be significantly associated with chronic ELF-EMF occupational exposure in prospective epidemiological studies (García et al., 2008; Davanipour and Sobel, 2009). Exposure to RF-EMFs has been reported to increase neuropsychiatric and behavioural disorders (Johansson et al., 2010; Divan et al., 2012), trigger cardiac rhythm alteration and peripheral arterial pressure instability (Havas, 2013; Saili et al., 2015), induce changes in immune system function (Lyle et al., 1983; Grigoriev et al., 2010; Sannino et al., 2011, 2014) and alter salivary (Augner et al., 2010) and

thyroid (Koyu et al., 2005; Mortavazi et al., 2009; Pawlak et al., 2014) function. There is an urgent need for more study of these diseases or biological alterations in relation to exposure to both ELF- and RF-EMFs.

4. An emerging concern: cognitive and neurobehavioral problems in children

Children, and especially fetuses, are more vulnerable than adults for most environmental exposures (Sly and Carpenter, 2012). This is because their cells are rapidly dividing and their organ systems are not mature. As a result, events that perturb cellular function early in life can result is abnormalities that last. There is a building body of evidence indicating that exposure to RF-EMFs has adverse effects on cognition and neurobehavior, especially in children and adolescents. Concern about the particular sensitivity of children to RF-EMFs emitted from mobile phone was first raised in 2000 by a British independent expert group (IEG, 2000) that noted that the increased sensitivity to EMFs of children could be due not only to the natural vulnerability of the developing nervous system, but also to the smaller head size and thickness of the skull. These factors, plus the higher conductivity of the young nervous system, result in greater penetration of RF-EMFs into the brain (Gandhi et al., 1996). Of concern is the fact that any adverse effects during development may have life-long consequences and that young people, because they will have a longer life span, will receive a greater cumulative exposure than adults (Kheifets et al., 2005; Hansson Mild et al., 2006).

There are several reasons to be concerned. Animal studies have shown that *in utero* RF-EMF exposure from mobile phones affects fetal programming and leads to alteration in neurodevelopment and behavior of offsprings (Aldad et al., 2012; Zhang et al., 2015). Exposure of young rats to non-thermal intensities impairs learning and spatial memory secondary to a deleterious impact of EMFs on hippocampal, pyramidal or cortical neurons. Similar detrimental cognitive and behavioural defects were also observed in adult animals exposed to low-intensity.

EMFs (Bas et al., 2009; Deshmukh et al., 2015; Kumari et al., 2017; Shahin et al., 2017). The exposure induces markers of oxidative stress and inflammation in the brain (Dasdag et al., 2012; Megha et al., 2015).

There are human data consistent with these animal studies. Divan et al. (2008) reported that prenatal and to a lesser degree postnatal exposure to cell phones is associated with emotional and hyperactivity problems in 7-year old children. This finding was confirmed in a second replicative study involving different participants (Divan et al., 2012). Birks et al. (2017) used data from studies in five cohorts from five different countries (83,884 children) and concluded that maternal mobile phone use during pregnancy increased the risk that the child will show hyperactivity and inattention problems. A meta-analysis involving 125,198 children (mean age 14.5 years) reported statistically significant associations between access to and use of portable screen-based media devices (e.g. mobile phones and tablets) and inadequate sleep quality and quantity and excessive daytime sleepiness (Carter et al., 2016). Early life exposure to lead has long been known to cause a reduction in cognitive function and shortened attention span (Needleman et al., 1979). Two studies have shown that prenatal (Choi et al., 2017) or postnatal (Byun et al., 2017) mobile phone exposure results in greater neurobehavioral effects in children with elevated lead levels than those seen with elevated lead alone. These results raise concern that EMFs may have synergistic actions with other environmental contaminants known to cause a reduction in intelligence quotient (IQ) and attention, such as polychlorinated biphenyls, methyl mercury, environmental tobacco smoke and probably others (Carpenter, 2006).

Finally the problem should be considered at the societal, worldwide level. Many adolescents (Lenhart, 2015) and even very young children and infants (Kabali et al., 2015) use cordless devices immoderately, to such a point that the common intensive use of devices in children and adolescents has been ascribed as an addiction (Paz de la Puente and Balmori, 2007; Roberts et al., 2014).

The specific absorption rate (SAR)-based ICNIRP safety limits were established on the basis of simulation of EMF energy absorption using standardized adult male phantoms, and designed to protect people only from the thermal effects of EMFs. These assumptions are not valid for two reasons. Not only do they fail to consider the specific morphological and bioclinical vulnerabilities of children, but also they ignore the effects known to occur at non-thermal intensities. The same criticisms apply to other so called “independent” advisory groups or agencies, such as the Advisory Group of Non-Ionizing Radiation in the UK (AGNIR, 2012), the French Agency for Food, Environmental and Occupational Health & Safety in France (ANSES, 2013), and the Scientific Committee on Emerging Newly Identified Health Risk (SCENIHR, 2009), all of whom deny the detrimental health effects of low intensity, non thermal EMF exposure and make recommendations based only on thermal SAR considerations.

Although several scientific authorities, such as the US American Academy of Pediatrics (AAP, 2013), and the Russian National Committee on Non-Ionizing Radiation Protection (RNCNIRP, 2011) have made specific recommendations to not allow the use of mobile phones by children and to limit their use by adolescents, unfortunately these age categories remain a target for marketing of mobile phone devices [http://www.who.int/peh-emf/project/mapnatreps/RUSSIA%20report%202008.pdf]. The RNCNIRP has warned that if no rational, health-based safety limits are adopted for children and adolescents and no measures are taken to limit the use of cordless devices, we can expect disruption of memory, decreases in learning and cognitive capabilities, increases in irritability, sleep disturbance, and loss of stress adaptation in this population. There will also be long-term effects, including an increase in brain cancer, infertility, EHS, Alzheimer disease and other neurodegenerative diseases (RNCNIRP, 2011; Markov and Grigoriev, 2015). National and international bodies, particularly the WHO, will bear major responsiblity for failing to provide specific science-based guidance and recommendations so as to avoid such global health threats.

5. Electrohypersensitivity, microwave illness or idiopathic environmental intolerance attributed to electromagnetic fields

There is a segment of the human population that is unusually intolerant to EMFs. The term “electromagnetic hypersensitivity” or “electrohypersensitivity (EHS)” to describe the clinical conditions in these patients was first used in a report prepared by a European group of experts for the European Commission (Bergqvist et al., 1997). Santini et al. (2001, 2003) reported similar symptoms occurring in users of digital cellular phones and among people living near mobile phone base stations.

In 2004, because of the seemingly increasing worldwide prevalence, WHO organized an international scientific workshop in Prague in order to define and characterize EHS. Although not acknowledging EHS as being caused by EMF exposure, the Prague working group report clearly defined EHS as “a phenomenon where individuals experience adverse health effects while using or being in the vicinity of devices emanating electric, magnetic or electromagnetic fields” (www.who.int/pehemf/EHS_Proceedings_June2006.pdf). Following this meeting, WHO acknowledged EHS as an adverse health condition (WHO, 2005).

According to the Prague Workshop recommendations, it was proposed to use the term “idiopathic environmental intolerance (IEI) attributed to electromagnetic fields” (IEI-EMF) because of the lack of a proven causal link with EMF exposure (Hansson Mild et al., 2006). This pathological disorder is identical to what has been previously described under the term “microwave illness” (Carpenter, 2015).

This syndrome is characterized by fatigue, chronic pain and impaired cognitive function (see the Paris appeal, http://appel-de-paris.com/?lang=en). The precise mechanism(s) whereby environmental exposure to either ELF- or RF-EMFs can cause the development of this syndrome are still uncertain. However several lines of experimental and clinical data are sufficiently strong so as to indicate that ELF-EMFs and RF-EMFs exposure is associated with adverse biological and clinical health effects in humans as well as animals (Rea et al., 1991; McCarty et al., 2011; Belpomme et al., 2015; Hedendahl et al., 2015; Irigaray et al., 2018a). The prevalence of EHS has been estimated to range 1–10% in developed countries (Hallberg and Oberfeld, 2006) but appears today to be around 3% (Huang et al., 2018).

Since WHO official reports on mobile phone exposure and public health (WHO, 2014) and more particularly on EHS (WHO, 2005), much clinical and biological progress has been made to identify and objectively characterize EHS, as was summarized during the international scientific consensus meeting of the 5th Paris Appeal Congress that took place in May 2015 in Brussels at the Royal Belgium Academy of Medicine (ISD, 2015). EHS has many characteristics in common with other IEI pathological disorders, including chronic fatigue syndrome, fibromyalgia, Gulf War Illness and especially the syndrome of multiple chemical senssitvity (MCS), which Belpomme et al. (2015) have shown to be associated with EHS in many patients who report being electrohypersensitive.

5.1. Bioclinical identification and characterisation of electrohypersensitivity

In a prospective study involving systematic face-to-face questionnaire-based interviews and clinical physical examinations of nearly two thousand patients who self-reported having EHS or EHS and MCS, Belpomme and colleagues reported that EHS is a well-defined clinico-biological entity, characterized by the progressive occurrence of neurologic symptoms, including headache, tinnitus, hyperacusis, superficial and/or deep sensibility abnormalities, fibromyalgia, vegetative nerve dysfunction and reduced cognitive capability. These symptoms are repeatedly reported by the patients to occur each time they are exposed to EMFs, even of weak intensity. They result in chronic insomnia, fatigue, emotional lability and depressive tendency (Belpomme et al., 2015; Irigaray et al., 2018b).

Table 4 presents the detailed symptomatic picture which was obtained during face-to-face interviews with subjects with EHS in comparison to those with both EHS and MCS and to a series of apparently healthy control subjects that showed no evidence of EHS and/or MCS. As shown in the Table, the symptoms reported are consistent with those in other published questionnaire-based studies of EHS patients (Dodge, 1970; Johansson et al., 2010; Nordin et al., 2014; Medeiros and Sanchez, 2016; Röösli, 2008). The clinical symptoms observed in EHS or EHS/MCS patients are statistically significantly much more frequent that those in apparently normal controls. Although many of these symptoms are non-specific, the general clinical picture resulting from their association and frequency strongly suggests that EHS can be recognized and identified as a specific neurological disorder.

Because of the multiple and relatively common symptoms and the lack of recognized objective diagnosis criteria, studies on EHS were left with only the patient's self-reported interpretation for many years. As a result, EHS has unfortunately been considered to be a psychiatric disease of unknown origin. This helps explain why most mainstream public health and societal bodies claim there is not sufficient data proving that the clinical symptoms experienced and reported by EHS patients are caused by EMF exposure. Therefore they refuse to acknowledge EHS as a true neuropathological disorder. This negative point of view was supported by some blind or double blind studies showing that most individuals who report they suffer from EHS were not able to identify when they were exposed to either EMFs or sham controls (Rubin et al., 2011; Eltiti et al., 2015). However other studies have found that EHS subjects can identify EMF exposure in a statistically significant manner when they are blinded to whether or not the exposure was on (Rea et al., 1991; McCarty et al., 2011).

To account for these seemingly negative results a nocebo effect was suggested (ANSES, 2017). However there is presently no consensus on a biological mechanism through which a nocebo effect could occur (Medeiros and Sanchez, 2016; Chrousos and Gold, 1992; Jakovljevic, 2014). Moreover, results obtained in a carefully designed psycho-clinical study in self-reporting EHS patients are not consistent with an initial nocebo response to perceived EMF exposure, even though it is plausible that after the onset of the disease such phenomena may intervene secondarily through an acquired learning and conditioning process (Dieudonné, 2016). In addition, a meta-analysis of cross sectional studies has documented a 38% greater risk of development of headaches among mobile phone users than non-users, and an increasing risk of headache with longer daily call duration (Wang et al., 2017).

Belpomme, Irigaray and colleagues recently identified several biomarkers in EHS and/or MCS patients which allow physicians to identify and objectively characterize EHS as a true somatic pathological disorder, discounting the hypothesis of a causal psychosomatic or nocebo-related process. These came in part from a prospective clinical and biological analysis of a series of several hundred consecutive cases of individuals who self-reported that they suffered from EHS or both EHS and MCS (Belpomme et al., 2015) and more recently from the prospective anlaysis of an additional series of EHS patients (Irigaray et al., 2018a). Table 5 summarizes the different biomarkers that have been measured in the peripheral blood of these patients and the results which have been obtained based on the EHS and EHS/MCS patient groups. Note that among the different markers, the 6-hydroxymelatonin sulfate/creatinine ratio in urine appears to be the best marker to be used in medical practice since it has been found to be decreased in all cases evaluated to date (Belpomme et al., 2015).

By measuring different major oxidative stress-related biomarkers, such as thiobarbituric acid reactive substances (TBARS), oxided glutathione (GSSG) and nitrotyrosine (NTT) in EHS patients, Irigaray et al. (2018b) have recently shown that near 80% of the EHS patients present with detectable oxidative stress biomarkers (Fig. 1). More than 40% of EHS patients present with at least one positive biomarker, 20% with two and 15% will all three of the biomarkers investigated. This indicates that in addition to the inflammation-related biomarkers previously associated with EHS, EHS patients are also characterized by exhibiting biomarkers of oxidative stress (Belpomme et al., 2015; Irigaray et al., 2018a,b).

The significance of the different biomarkers measured in the peripheral blood of EHS and EHS/MCS patients is that these results imply that these patients present with some degree of oxidative/nitrosative stress, inflammation and autoimmune response. Increased levels of several of these markers (notably protein S100B and NTT) may reflect hypoxia-associated oxidative stress-induced blood brain barrier (BBB) opening. It has been previously hypothesized that opening of the BBB can be caused by environmental

Table 4
Clinical symptom occurrence in EHS and EHS/MCS patients in comparaison with normal controls[a].

	EHS	EHS/MCS	p[b]	Normal controls	p[c]	p[d]
Headache	88%	96%	0.065	0%	<0.0001	<0.0001
Dysesthesia	82%	96%	0.002	0%	<0.0001	<0.0001
Myalgia	48%	76%	<0.0001	6%	<0.0001	<0.0001
Arthralgia	30%	56%	<0.001	18%	0.067	<0.0001
Ear heat/otalgia	70%	90%	<0.001	0%	<0.0001	<0.0001
Tinnitus	60%	88%	<0.0001	6%	<0.0001	<0.0001
Hyperacousis	40%	52%	0.118	6%	<0.0001	<0.0001
Dizziness	70%	68%	0.878	0%	<0.0001	<0.0001
Balance disorder	42%	52%	0.202	0%	<0.0001	<0.0001
Concentration/Attention deficiency	76%	88%	0.041	0%	<0.0001	<0.0001
Loss of immediate memory	70%	84%	0.028	6%	<0.0001	<0.0001
Confusion	8%	20%	0.023	0%	0.007	<0.0001
Fatigue	88%	94%	0.216	12%	<0.0001	<0.0001
Insomnia	74%	92%	0.001	6%	<0.0001	<0.0001
Depression tendency	60%	76%	0.022	0%	<0.0001	<0.0001
Suicidal ideation	20%	40%	0.003	0%	<0.0001	<0.0001
Transitory cardiovascular abnormalities	50%	56%	0.479	0%	<0.0001	<0.0001
Occular deficiency	48%	56%	0.322	0%	<0.0001	<0.0001
Anxiety/Panic	38%	28%	0.176	0%	<0.0001	<0.0001
Emotivity	20%	20%	1	12%	0.176	0.176
Irritability	24%	24%	1	6%	<0.001	<0.001
Skin lesions	16%	45%	<0.0001	0%	<0.0001	<0.0001
Global body dysthermia	14%	8%	0.258	0%	<0.0001	<0.007

[a] This data results from the clinical analysis of the 100 first clinically evaluated cases issued from the already published series of EHS and/or MCS patients who have been investigated for biological markers [Belpomme et al., 2015]. It has been compared symptomatically with data obtained from a series of 50 apparently normal subjects matched for age and sex, used as controls.
[b] Significance levels (p values) obtained for compararison between the EHS and EHS/MCS groups.
[c] Significance levels (p values) obtained for compararison between the EHS and normal control groups.
[d] Significance levels (p values) obtained for compararison between the EHS/MCS and normal control groups.

Table 5
Patient mean values and standard deviations of biomarker levels in comparison with normal reference values as well as the percentage of patients with abnormal values in the peripheral blood in subjects with EHS or both EHS and MCS (Belpomme et al., 2015).

Biomarker and Normal reference values	Patients groups			
	EHS Mean ± SD	% Above normal	EHS/MCS Mean ± SD	% Above Normal[a]
hs-CRP < 3 mg/l	10.3 ± 1.9	15%	6.9 +/1.7	14.3%
Vitamine D > 30 ng/ml	20.6 ± 0.5	69.3%	14.5 ± 1.3	70.1%
Histamine< 10 nmol/l	13.6 ± 0.2	37%	13.6 ± 0.4	41.5%
IgE< 100 UI/ml	329.5 ± 43.9	22%	385 ± 70	24.7%
S100B < 0.105 μg/l	0.20 ± 0.03	14.7%	0.17 ± 0.03	19.7%
Hsp 70 < 5 ng/ml	8.2 ± 0.2	18.7%	8 ± 0.3	25.4%
Hsp 27< 5 ng/ml	7.3 ± 0.2	25.8%	7.2 ± 0.3	31.8%
Anti-O-myelin auto-antibodies[b]	Positive	22.9%	Positive	23.6%
24-h urine 6-OHMS/creatinine ratio >0.8[c]	0.042 ± 0.003	100%	0.048 ± 0.006	100%

hs-CRP, high-sensitivity C-reactive protein; IgE, Immunoglobulin E; S100B, S 100 calcium binding protein B; Hsp 27, heat shock protein 27; Hsp 70, heat shock protein 70; anti-O-myelin auto-antibodies, auto-antibodies against O-myelin; 6-OHMS, 6-hydroxymelatonin sulfate.
[a] There is no statistically significant difference between the two groups of patients for the different biomarkers analyzed, suggesting that EHS and MCS share a common pathological mechanism for genesis.
[b] Qualitative test.
[c] Data restricted to those not on neuroleptic medication as the simultaneous use of several psychotherapeutic drugs may also be associated with a decrease of this 24-h urine ratio by modifying melatonine metabolism.

stressors, be they chemicals or EMFs. This may have occurred in these patients, as has been shown to occur in several (but not all) animal experiments involving EMF exposure (Oscar and Hawkins, 1977; Persson et al., 1997; Eberhardt et al., 2008; Sirav and Seyhan, 2009). Comparable data using metabolic and genetic biomarkers were also obtained in another large series of EHS patients (De Luca et al., 2014). Overall these data indicate that the clinical use of biomarkers allows the objective characterisation and identification of EHS and MCS as two etiopathologic facets of a unique pathological disorder, and also allows insight into the genesis of these two diseases.

The development of new imaging techniques has also greatly increased our ability to objectively characterize EHS and MCS. Using ultrasonic cerebral tomosphygmography (UCTS) (Parini et al., 1984), EHS- and EHS/MCS-patients were found to have a statistically significant decrease in mean pulsometric index in several middle cerebral artery-dependant portions of the temporal lobes, especially in the capsulo-thalamic area, which is part of the limbic

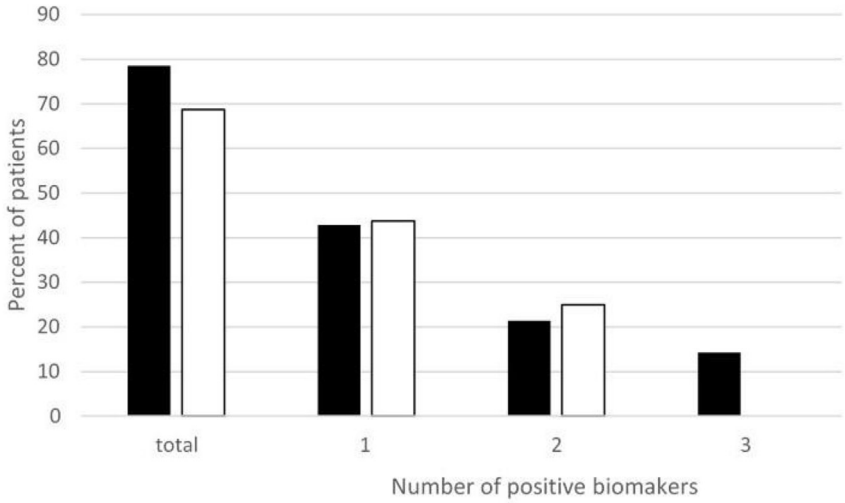

Fig. 1. Percentage of EHS self-reporting patients having positive TBARs, GSSG and/or NTT oxidative stress biomarkers measured in the peripheral blood. "Positive" biomarkers correspond to marker levels above the upper normal limit; "total" corresponds to the patients with one or more positive biomarker levels. Black bars show the percentage of patients with one, two or all three of the biomarkers for TBARS, GSSG and NTT. The white bars show the percentage of patients with either TBARs or GSSG or both oxidative stress markers.

system and the thalamus. This suggests that EHS and EHS/MCS may be associated with a brain blood flow (BBF) deficiency and/or neuronal dysfunction in these brain structures (Belpomme et al., 2015; Irigaray et al., 2018a,b). Irigaray et al. (2018c) have recently confirmed that UCTS is the best imaging technique to diagnose EHS and to follow patients treated for EHS and/or MCS.

In addition, using positron emission tomography (PET) it has been shown that short term exposure to pulse-modulated RF-EMF causally affects regional BBF in normal subjects using a mobile phone (Aalto et al., 2006; Huber et al., 2005), a finding that may account for the modifications observed in the sleep and waking EEG (Huber et al., 2002). By use of functional MRI (fMRI) in EHS patients exposed chronically to ELF-EMFs, regional BBF changes have been reported in the frontal lobes, such as abnormal default mode network and more particularly a decrease in BBF and cerebral metabolism. These observations indicate that fMRI may also be a tool for diagnosis of EHS and clinical follow up of patients (Heuser and Heuser, 2017). A decreased BBF-associated pulsometric index decrease in both hemispheres was also recently observed by the Belpomme group by using transcranial Doppler ultrasound (TDU) (Purlauastja and Sorond, 2012) applied to the middle cerebral artery in a study involving 120 EHS and/or MCS patients. This study revealed a decrease in pulsatility index and an increase in diastolic flow velocity in 70% of the 120 cases investigated to date.

In summary it is the strong opinion of the authors that there is presently sufficient clinical, biological and radiological data emanating from different independent international scientific research groups for EHS, whatever its causal origin, to be acknowledged as a well-defined, objectively characterized pathological disorder. As a result, patients who self-report that they suffer from EHS should be diagnosed and treated utilizing presently available objective biological tests, among which are the concentration of peripheral blood biomarkers and the use of imaging techniques such as PET, fMRI and TDU and, when available, UCTS. Whatever its etiological origin and mechanism of action, EHS should be acknowledge by the WHO as a real and distinct neurological and pathological disorder (McCarty et al., 2011; Hedendahl et al., 2015) and thus be included in the International Classification of Diseases.

5.2. Possible etiopathogenic processes involved in genesis of electrohypersensitivity

EMFs, both RF-EMFs at non-thermal intensities and ELF-EMFs, have been found to cause persistent adverse biological effects in microorganisms (Fojt et al., 2004), plants (Roux et al., 2008; Maffei, 2014), birds (Balmori, 2005; Balmori and Hallberg, 2007; Frey, 1993), and mammals. Therefore the effects observed in humans cannot be due to only a nocebo or psychosomatic effect. These biological effects may be due both to the pulsed and polarised characteristics of man-made EMFs emitted by electric or wireless technologies as opposed to the terrestrial non-polarised and continuously emitted natural EMFs (Blackman, 2009; Belyaev, 2015; Panagopoulos et al., 2015).

The inflammatory and oxidative/nitrosative states that have been documented in EHS patients are remarkable since they confirm the data obtained experimentally in animals exposed to non-thermal EMFs (Esmekaya et al., 2011; Burlaka et al., 2013), and especially in the brain (Megha et al., 2015; Kesari et al., 2011). The limbic system–associated capsulo-thalamic abnormalities that the Belpomme group has observed by using UCTS in EHS and/or MCS patients (Belpomme et al., 2015; Irigaray et al., 2018a,c) may likely correspond to the hippocampal neuronal alterations caused by EMF exposure in the rats (Bas et al., 2009; Furtado-Filho et al., 2015; Deshmukh et al., 2013). Fig. 2 summarizes our hypothesis regarding the inflammation and oxidative stress-related mechanisms which may account for EMF- and/or chemically-related health effects in the brain and consequently for EHS genesis.

6. Mechanisms whereby low intensity electromagnetic fields cause biological effects and harm

Arguments used in the past to attempt to discount the evidence showing deleterious health effects of ELF-EMFs and RF-EMF exposure at non-thermal SAR levels were based on the difficulties encountered in understanding the underlying biological effects and the lack of recognized basic molecular mechanisms accounting for these effects. This is no longer the case. There are a number of well-documented effects of low intensity EMFs that are the mechanistic basis behind the biological effects documented above (www.

bioinitiative.org). These include induction of oxidative stress, DNA damage, epigenetic changes, altered gene expression and induction including inhibition of DNA repair and changes in intracelluar calcium metabolism. Both low-intensity ELF-EMF and non-thermal RF-EMF effects depend on a number of physical parameters and biological variables and physical parameters, which account for the variation in health outcomes (Belyaev, 2015; Belyaev et al., 1999). Importantly, the most severe health effects are observed with prolonged chronic exposures even when intensities are very low (Belyaev, 2017). The physics of non-equilibrium and non-linear systems and quantum mechanics are at least in part the basis of the physical mechanisms responsible for the non-thermal molecular and biological effects of non-thermal EMF radiation (Belyaev, 2015), although a detailed report on these actions is beyond the scope of this review.

Lower RF-EMF intensity is not necessarily less bioactive or less harmful. Non-thermal EMF effects can be observed at intensities which are very close to ordinary background levels and quite similar to intensities emitted by mobile phone base stations. There are time windows for observation of non-thermal EMF effects which may be dependent upon the endpoint measured, the cell type and the duration and power density of exposure. Non-thermal RF-EMF effects are affected by static magnetic fields and electromagnetic stray fields, which result in the variation of non-thermal EMF effects from mobile phones because of adjacent electrical appliances, power lines and other sources of ELF and static magnetic fields, including changes in the geomagnetic field (Gapeev et al., 1999a and b).

Cell-to-cell interactions potentiate the response to non-thermal EMFs (Belyaev et al., 1996). Biological responses to EMFs have been shown to be influenced by sex and age (Zhang et al., 2015; Sirav and Seyhan, 2016). Physiological parameters such as the stage of cell growth, oxygen, divalent ions and temperature are important variables affecting cellular responses to EMFs (Liburdy and Vanek, 1987; Sannino et al., 2011).

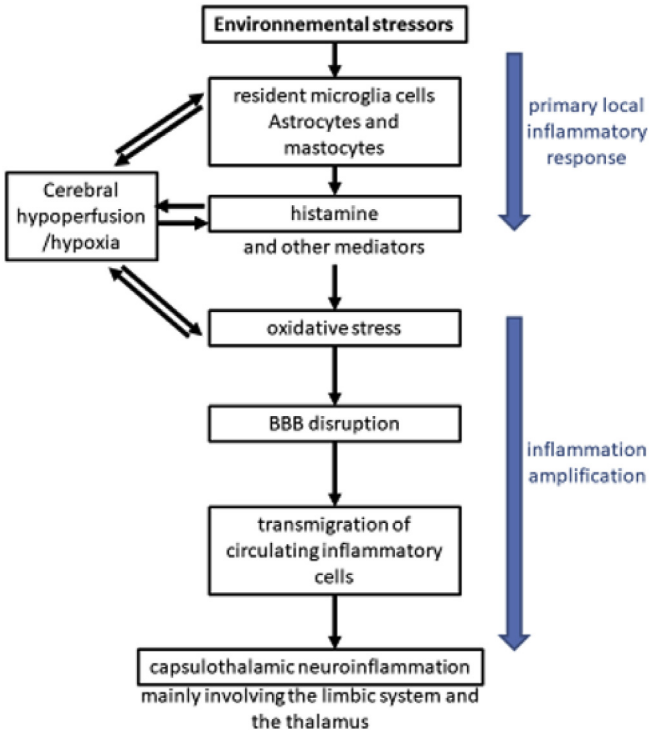

Fig. 2. Hypothetical EHS/MCS common etiopathogenic model based on neuroinflammation and oxidative/nitrosative stress-induced blood brain barrier disruption (Belpomme et al., 2015).

6.1. Combined exposures

EMFs at non-thermal intensities may interfere with other environmental stressors, showing an interplay of molecular pathways and resulting in either beneficial or detrimental health effects, depending on the nature and conditions of co-exposures (Novoselova et al., 2017; Ji et al., 2016). One example is the demonstration that RF-EMF exposure modulates the DNA damage and repair induced by ionizing radiation (Belyaev et al., 1993). Another example is the synergistic of exposure to lead and EMFs on cognitive function in children described above (Choi et al., 2017; Byun et al., 2017). These co-exposure factors should be considered when assessment of detrimental effects, including carcinogenicity, is performed.

Not all of the effects of EMFs on the nervous system and other organs are necessarily harmful. The best example of a positive effect is the well-documented and clinically useful benefit of applied magnetic fields to promote bone healing (Bassett, 1994). Both ELF-EMF (Zhang et al., 2015) and RF-EMF (Arendash et al., 2010) have been reported to slow cognitive decline in rodent models of Alzheimer's disease. Some human studies report a facilitating effects of cognitive performance (Lee et al., 2001) while Koivisto et al. (2000) reported an increase in response time and vigilance tasks but a decrease in mental arithmetic tasks. These studies clearly show that EMFs have biological effects at non-thermal intensities, but suggest that not all biological effects are necessarily harmful.

6.2. Duration of exposure and dose intensity

Such parameters as power density, dose, and duration of exposure have been analyzed for development of reliable safety standards, which would protect against the detrimental health effects of chronic exposure to RF-EMFs at non-thermal intensities. Some studies show no effect under fixed short-term exposures, but this does not imply that there are no effects from longer-term exposures (Choi et al., 2014). Exposure in studies showing RF-EMF effects was on average twice the duration as those with no significant effects (Cucurachi et al., 2013). The response to non-thermal EMFs depends on both power density and duration of exposure. Importantly, the same response is observed with lower power density but prolonged exposure as at higher power density and shorter exposure (Nordenson et al., 1994). While SAR is a good surrogate for thermal RF effects from acute exposures, many studies have shown that SAR should be either replaced by “dose-specific absorption” or power density complimented by duration of exposure for description of non-thermal RF effects (Belyaev, 2015). Recent studies have provided more evidence for the greater importance of dose and duration of exposure than SAR alone for biological and health effects from long-term exposures to non-thermal RF-EMFs (Furtado-Filho et al., 2015).

6.3. Oxidative stress

Non-ionizing radiation does not have sufficient energy to directly break chemical bonds, and therefore the DNA damage that occurs with non-ionizing EMF exposures is primarily a consequence of generation of reactive oxygen species (ROS), resulting in oxidative stress. There are numerous animal experiments which clearly demonstrate that non thermal EMFs can cause oxidative stress (Esmekaya et al., 2011; Burlaka et al., 2013), particularly in the brain (Shahin et al., 2017; Dasdag et al., 2012; Megha et al., 2015; Furtado-Filho et al., 2015). Oxidative stress is known to

play a central role in development of cancer and aging and serves as a signaling agent in the inflammatory response (Holmstrom and Finkel, 2014).

The brain is a particularly important organ for sensitivity to EMFs. Brain cancer resulting from EMF exposures is a serious concern, and EHS is a disease of the central nervous system. Several mechanisms at the cellular and molecular levels have been reported that may be the basis of these non-thermal RF-EMF effects on brain function. ELF- and/or RF-EMF exposure at embryonic or early postnatal stages can alter *in vivo* synaptic efficacy and plasticity of neurons (Balassa et al., 2014), a finding which was further supported by *in vitro* studies showing a significant decrease in the differentiation of neural stem cells into neurons (Eghlidospour et al., 2017), the alteration of transcript levels of neuronal differentiation-related genes and impairment of neurite outgrowth of embryonic neural stem cells exposed to ELF- or RF-EMFs (Ma et al., 2014). These observations support the conclusion that low-intensity but prolonged exposure to non-thermal EMFs may have adverse effects on neurogenesis during development and indicate how important it is to protect the fetus and young child from excessive exposure to all mobile devices.

Animal studies have documented that 900 MHz or 2.45 GHz non thermal RF-EMF exposure in rats, either short term or chronic, can trigger neuronal dysfunction and even apoptosis of hippocampal pyramidal cells (Bas et al., 2009; Shahin et al., 2017) and cerebellum Purkinje cells (Sonmez et al., 2010) through induction of oxidative stress. Exposure of pregnant dams elicited EMF oxidative stress-induced neuronal pathologic changes in offspring (Odaci et al., 2016). Such pathological changes could be due to ROS-induced opening of the BBB (Nordal and Wong, 2005) and/or to ROS-associated brain hypoxia caused by a decrease in EMF-induced BBF and/or EMF-induced hemoglobin deoxygenation (Mousavy et al., 2009; Muehsam et al., 2013). The resulting hypoxia may induce metabolic neuronal dysfunction as in the case of EHS patients (Belpomme et al., 2015) but also neuronal cell death by either apoptosis or necrosis as in the case of Alzheimer's disease and other forms of dementia (Bell and Zlokovic, 2009).

While some consider the laboratory data on EMFs as being inconsistent, showing either detrimental or no effects and on occasion even beneficial effects, the vast majority still show detrimental effects. For example Henry Lai in the Bioinitiative Report Research Summaries Update of November 2017, Chapter 6 on Genotoxic Effects, reported that i) of 46 studies on ELF genotoxicity with the comet assay as the end point, 34 studies (74%) showed detrimental effects, ii). Of 189 total studies on ELF and oxidative stress, 162 (87%) showed a positive correlation, and iii) of 200 studies on RF and free radicals, 180 (90%) showed detrimental effects. One reason for variability between laboratory studies is the strong dependence on low-threshold EMF effects on a number of physical and biological variables (Belyaev, 2010).

6.4. Genetic and epigenetic mechanisms

Genetic effects are the most direct cause for carcinogenicity. This is true both for genotoxic changes caused by exposure to EMFs and existing polymorphic genetic differences within a population that increase susceptibility to cancer. DNA can no longer be considered to be unaffected by environmental EMF levels, as many studies have shown that DNA can be activated and damaged by EMFs at levels that have been considered to be safe (Blank and Goodman, 1999).

The primary mechanism through which low-intensity EMFs can alter DNA is through ROS production. Lai and Singh (2004) first reported that a 2 h exposure of rats to 60 Hz EMFs at 0.1–0.5 mT resulted in DNA strand breaks in neurons, and provided evidence that this effect was mediated by free radical formation and blocked by free radical scavengers. Vijayalaxmi and Prihoda (2009) in a meta-analysis of 87 publications found a biologically small but statistically significant difference between DNA damage in ELF-EMF-exposed somatic cells as compared to controls, and reported evidence for epigenetic changes for some outcomes. For ELF-EMFs this breakage effect was stronger when exposure was intermittent rather than continuous (Nordenson et al., 1994).

Yang et al. (2008) have reported an OR = 4.31 (95% CI = 1.54–12.08) for leukemia in children living within 100 m of a high voltage powerline if they had a certain polymorphism of a DNA repair gene.

Exposure to RF-EMFs can also induce DNA damage under specific conditions (Markova et al., 2005). Tice et al. (2002) and Vijayalaxmi et al. (2013) reported DNA damage and micronuclei formation in cultured human leukocytes and lymphocytes upon exposure to RF-EMF signals of at least 5 W/kg. Not all cell types showed similar responses. Schwartz et al. (2008) reported micronucleus changes in fibroblasts but not lymphocytes exposed to 1950 MHz EMFs. Kesari et al. (2014) also demonstrated DNA strand breaks in the brains of rats exposed for 2 h per day for 60 days to a 3G mobile phone. Changes in DNA secondary structure (Semin, 1995; Diem et al., 2005) and chromosome instability (Mashevich, 2003) have been observed upon exposure to RF-EMFs emitted by mobile phones.

Epigenetic changes, rather than genetic changes in DNA, may underlie many or even most of the biological effects of non-thermal EMFs (Sage and Burgio, 2017). Non-thermal EMFs are epigenetic stressors which can alter gene expression by acting through physical or biochemical processes and be reflected as chromatin remodeling (Belyaev et al., 1997), histone modification (Wei et al., 1990) or altered microRNA (Dasdag et al., 2015) at intensities far below those that cause measureable tissue heating.

Chromatin plays a key regulatory role in controlling gene expression and, more particularly, the access of transcription factors to DNA. It has been shown that extremely low intensity RF-EMF exposure, i.e. at intensities comparable to that of mobile phone and towers, results in changes in chromatin conformation and gene expression (Belyaev et al., 1997; Belyaev and Kravchenko, 1994; Belyaev et al., 2006; Belyaev et al., 2009). In a large number of cells and tissues, compaction of chromatin in specific loci may lead to gene silencing, loss of histone regulatory effects and DNA repair capacity (Wei et al., 1990). Belyaev and collaborators (Markova et al., 2005; Belyaev et al., 2009) have shown that exposure to RF-EMFs emitted by GSM mobile phone alters chromatin conformation in human lymphocytes and inhibits formation of p53-binding protein 1 (53BP1) and phosphorylated histone H2AX (γ-H2AX) DNA repair foci.

EMFs in both the ELF and RF ranges may epigenetically affect DNA by inducing the expression of stress response genes and consequently the synthesis of chaperone stress proteins (Blank and Goodman, 2011a and b). A specific gene sequence has been identified that acts as a sort of antenna, specifically sensitive and responsive to EMFs (Blank and Goodman, 2011b). This is a gene sequence coding for HSP70, a protein belonging to a family of conserved, ubiquitously expressed “heat shock proteins” that sense danger signals and protect cells from the most disparate stress conditions. This is an unambiguous demonstration that EMF exposure even at non-tissue heating intensities has the potential to be harmful to cells and organisms. The HSP70 promotor contains different DNA regions that are specifically sensitive to diverse stressors, thermal and non-thermal. The EMFs are specifically perceived by the sequences sensitive to non-thermal stimuli. During the process of HSP70-response induction, EMFs can activate directly the HSP70 gene promoter (Rodrequez-De la Fuente et al.,

2010) which contains a magnetic field-responsive domain (Lin et al., 1999, 2001).

EMF-related HSP70 and HSP27 stress responses have been detected in the hippocampus of rats exposed to non-thermal EMFs (Yang et al., 2012). Shahin et al. (2017) reported that mice exposed to 2G mobile phones continuously for four months showed elevated ROS, lipid peroxidation, total nitrate and nitrite concentrations and malondialdehyde levels in homogenates of different tissues, and decreased levels of several antioxidant enzymes. These observations justify the use of these markers to characterize EHS in patients who report that they are sensitive to EMFs.

The EMF effects have been suggested to be mediated by the mitogen-activated protein kinase (MAPk) cascades, which is a central signaling transduction pathway which governs all stress-related cellular processes occurring in response to extracellular stimuli (Friedman et al., 2007). It has been shown that long term exposure of cells to mobile phone frequencies or to ELF-EMFs (Goodman et al., 2009) activates the extracellular-signal regulated kinase (ERK), which is one of the four MAPk cascades so far identified.

Non-thermal RF-EMFs may also alter expression of other genes. As long ago as Byus et al., 1988 showed that 450 MHz RF increased ornithine decarboxylase activity in hepatoma cells. Markova et al. (2005) exposed human fibroblasts and mesenchymal stem cells to mobile phone RF-EMFs with analysis of tumor suppressor p53 binding protein 1. Formation of 53BP1 foci was inhibited in both cells types, but the stem cells always showed a greater response. Fragopoulou et al. (2011) exposed mice to either a typical mobile phone or a wireless DECT base station and analyzed the brain proteome. They found significant alteration in 143 specific proteins (ranging from a 0.003 fold downregulation to up to a 114-fold overexpression.) Luo et al. (2013) exposed pregnant women undergoing a first trimester abortion to a mobile phone applied to the abdomen and performed a proteomic analysist of placental villous tissue. They report 15 proteins which were significantly altered by at least 2- to 2.5-fold in exposed women as compared to control women. Twelve of these proteins were identified. Yan et al. (2008) exposed rats to mobile phones 6 h per day for 126 days, and found upregulation of specific mRNAs that regulated several proteins, including calcium ATPase, neural cell adhesion molecule, neural growth factor and vascular endothelial growth factor. EMFs at non thermal levels may not only alter the expression of many proteins but also may directly affect protein conformation (Fragopoulou et al., 2011; Bohr and Bohr, 2013; Beyer et al., 2013) and modify enzyme activity (Vojisavljevic et al., 2010), so altering the regulating capacity of the epigenome. These are epigenetic, not genetic, effects (Sage and Burgio, 2017).

Non-thermal EMF exposure can epigenetically interfere with the differentiation and proliferation programs of stem cells in fetal and adult tissues through ROS production (Wolf et al., 2007; Falone et al., 2007; Ayşe et al., 2010; Park et al., 2014). Stem cells are the most sensitive cells to EMF exposure (Eghlidospour et al., 2017; Markova et al., 2010) and this is particularly the case for neural stem cells of the hippocampus (Leone et al., 2014).

The endogenous natural ionic currents and electrical fields in the human body (Jaffe and Nuccitelli, 1977) are vulnerable to the oscillary properties of non-thermal EMFs. These consequently may cause detrimental effect on cell differentiation and proliferation in adult tissues (Levin, 2003) in addition to the effects on cell differentiation, proliferation and migration in the fetus (Wolf et al., 2007; Ayşe et al., 2010; Leone et al., 2014). Fetal programming cannot be reduced to only genetic programs. Developmental processes are essentially epigenetic (Leone et al., 2014), and exposure to epigenetic stressors such as non-thermal EMFs are much more dangerous for the fetus than for the adults.

6.5. Calcium regulation

There has long been evidence that EMFs alter several aspects of calcium function. This is important because calcium regulates many different aspects of cell function. Bawin and Adey (1976) reported that very weak ELF-EMFs trigger efflux of calcium from isolated chick brain, although the implications of this observation were not clear. Later they reported a similar action of RF-EMFs (Adey et al., 1982). Pulsed low-frequency EMFs promote bone healing and promote calcium uptake into bone (Spadaro and Bergstrom, 2002) and osteoblasts (Zhang et al., 2010). 50 Hz EMFs increase the number of voltage-gated calcium channels in neuroendocrine cells (Grasso et al., 2004) and presynaptic nerve cell terminals (Sun et al., 2016). Wei et al. (2015) found that ELF-EMFs also altered the frequency of calcium transients in cardiomyocytes and decreased calcium concentrations in sarcoplasmic reticulum. These changes in calcium in heart muscle may be the basis for the cardiovascular effects reported in humans on exposure to EMFs (Havas, 2013). In spite of numerous studies reporting altered calcium metabolism upon exposure to both ELF- and RF-EMFs, the overall implications of these effects are still not clear. However, some have suggested (Ledoigt and Belpomme, 2013) that calcium activation of proteins could be the initial event that results in altered protein configuration, leading to generation of ROS and ultimately activating the molecular pathways to cancer.

7. Public Health Implications of Human Exposure to EMFs

The incidence of brain cancer in children and adolescents has increased between 2000 and 2010 (Ostrom et al., 2015). Gliomas are increasing in the Netherlands (Ho et al., 2014), glioblastomas are increasing in Australia (Dobes et al., 2011) and England (Philips et al., 2018) and all brain cancers are increasing in Spain (Etxeberrua et al., 2015) and Sweden (Hardell and Carlberg, 2017). The latency period between initial exposure and clinical occurrence of brain cancer is not known but is estimated to be long. While not all reports of brain cancer rates show an increase, some do. The continually increasing exposure to EMFs from all sources may contribute to these increases. The prevalence of EHS is unknown, but various reports suggest that it is between 1 and 10% of the population (Hallberg and Oberfeld, 2006; Huang et al., 2018). Male fertility has been declining (Geoffroy-Siraudin et al., 2012; Levine et al., 2017). EMFs increase the risk of each of these diseases and others. Alzheimer's disease is increasing in many countries worldwide and its association with ELF-EMF occupational exposure has been clearly demonstrated through several independent epidemiological studies (Davanipour and Sobel, 2009; Sobel et al., 1996; Qiu et al., 2004) and a meta-analysis of these studies (García et al., 2008). A recent meta-analysis (Huss et al., 2018) has reported an increased risk of amyotrophic lateral sclerosis in workers occupationally exposure to ELF-EMFs.

Safety limits for RF exposure have been based (until today) on the thermal effects of EMFs. But these standards do not protect people, particularly children, from the deleterious health effects of non-thermal EMFs (Nazıroğlu et al., 2013; Mahmoudabadi et al., 2015). Each of these diseases is associated with decrements in health and quality of life. Brain cancer patients often die is spite of some improvement in treatment, while EHS patients present with increased levels of distress, inability to work, and progressive social withdrawal. The ability for humans to reproduce is fundamental for the maintenance of our species.

The scientific evidence for harm from EMFs is increasingly strong. We do not advocate going back to the age before electricity or wireless communication, but we deplore the present failure of public health international bodies to recognize the scientific data

showing the adverse effects of EMFs on human health. It is encouraging that some governments are taking action. France has removed WiFi from pre-schools and ordered Wi-Fi to be shut off in elementary schools when not in use (http://www.telegraph.co.uk.news/2017/12/11/france-ipose-total-ban-mobile-phones-schools/). The State of California Department of Public Health has issued a warning on use of mobile phones and offered advice on how to reduce exposure (State of California, 2017). There are many steps that are neither difficult nor expensive that can be taken to use modern technology but in a manner that significally reduces threats to human health.

It is urgent that national and international bodies, particularly the WHO, take this significant public health hazard seriously and make appropriate recommendations for protective measures to reduce exposures. This is especially urgently needed for children and adolescents. It is also important that all parts of society, especially the medical community, educators, and the general public, become informed about the hazards associated with exposure to EMFs and of the steps that can be easily taken to reduce exposure and risk of associated disease.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.envpol.2018.07.019.

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