Adverse Health Effects from Radiofrequency (RF) Radiation with a Focus of AMI Meters

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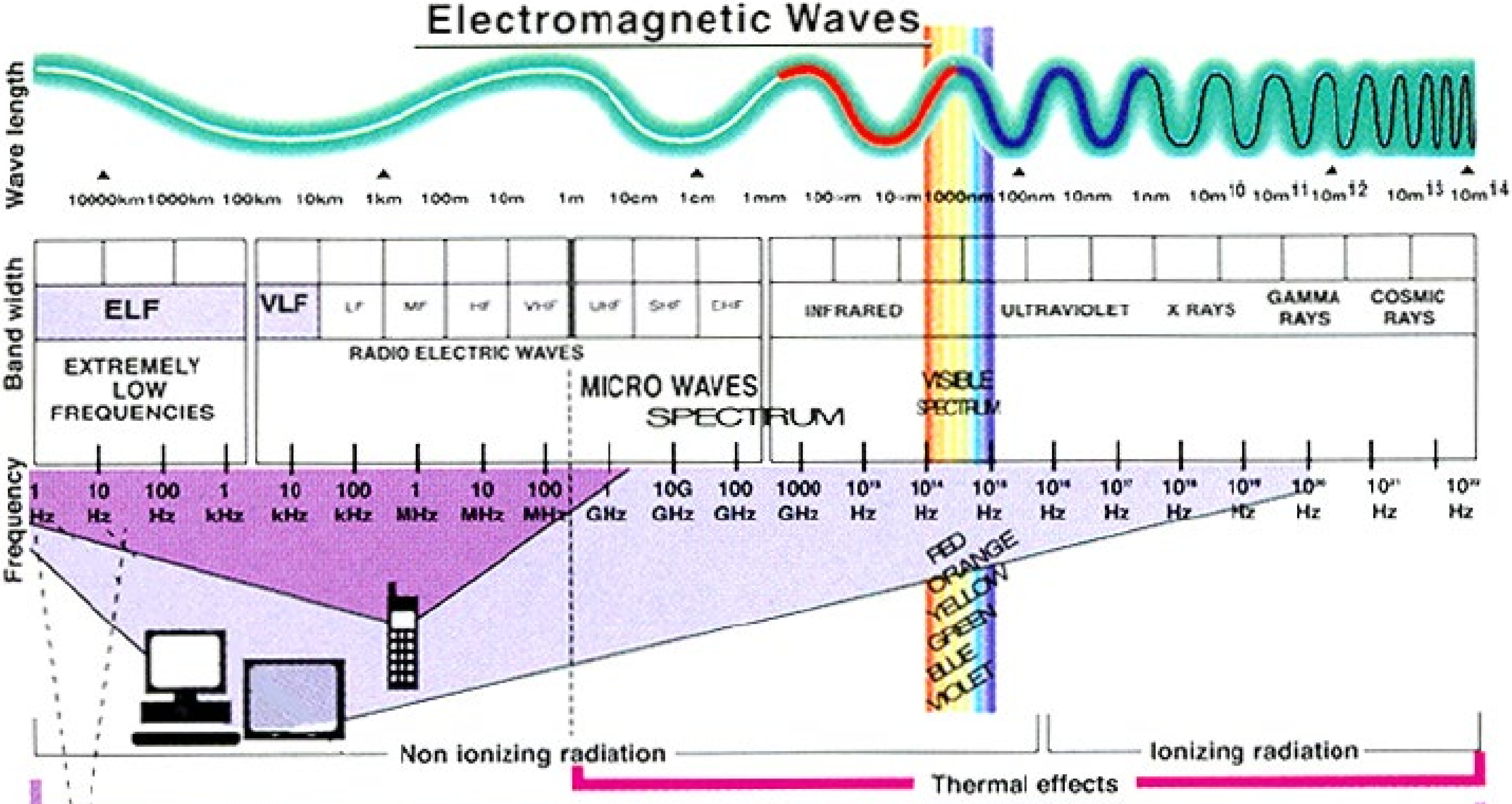
Who Am I?

- I am David O. Carpenter, a public health physician who received both AB and MD degrees from Harvard University. I chose public health and research over clinical practice.
- My initial involvement of electromagnetic field (EMF) effects was during my tenure as Chair of the Neurobiology Department at the Armed Forces Radiobiology Research Institute in Bethesda. I then became the Director of the Wadsworth Center for Laboratories and Research at the New York State Department of Health, where one of my responsibilities was to administer a research program on health effects of magnetic fields coming from electricity. After that program ended I became the spokesperson for EMF issues in New York State until I moved to the University at Albany as Dean of the School of Public Health. When I stepped down as Dean I became the Director of the Institute for Health and the Environment, which has been designated as a Collaborating Center of the World Health Organization, a position I hold today.

Electromagnetic spectrum



Radiofrequency (RF) EMFs

- These are the communications frequencies, ranging from AM and FM radio, TV, mobile phones, and radar.
- WiFi, AMI smart meters and wireless anything use RF fields to communicate between a generator and a receiver.
- Driverless automobiles will use EMFs for navigation.
- Microwave ovens use RF. The fact that you can cook your potato in a microwave over is proof that communication frequencies can have biological effects.

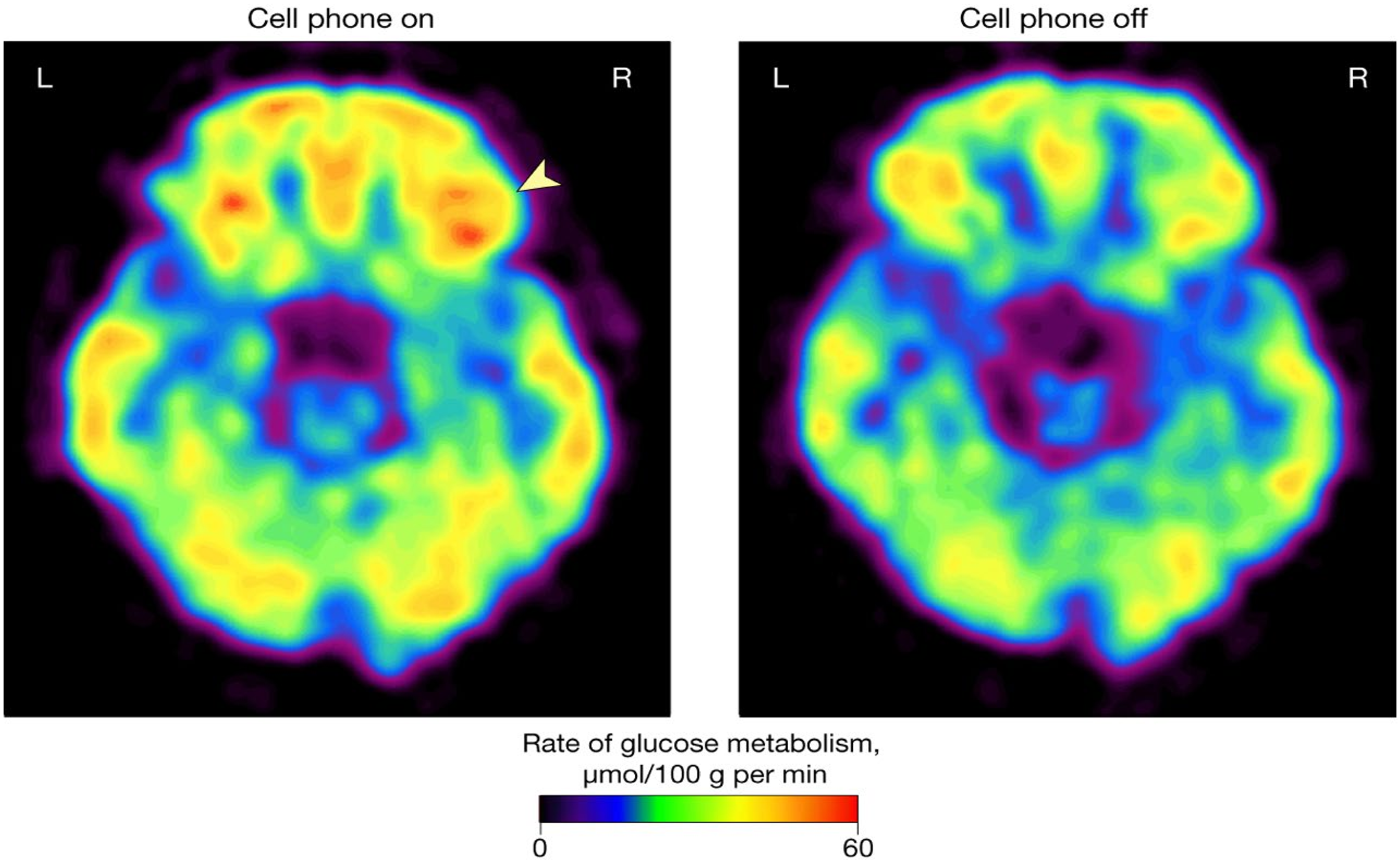
Safety Standards for Exposure to RFR.

- In the US it is the Federal Communications Commission that has this responsibility. Almost all members come from the industry. They have absolutely no health expertise.
- The position of the FCC is that the only concern due to RF radiation is tissue heating, like that you get from your microwave oven.
- There are thousands of scientific studies showing adverse effects at much lower intensities than those causing tissue heating.
- While the average RF emission from a AMI meter does not exceed the FCC guidelines it is sufficient to cause adverse health effects in some people.

Health Risks to Humans From Existing Cell Phone Radiofrequency Radiation

- Cancer:
  - Brain Cancer: Gliomas on the side of the head where the cell phone is normally used and glioblastoma, a very dangerous cancer that is almost always fatal.
  - Acoustic neuroma, a Schwannoma of the auditory nerve. This is a tumor, not a cancer, but in a bony canal.
  - Cancer of the parotid gland and thyroid gland in the cheek and throat, near to where a cell phone is used.
  - Probably other kinds of cancer, depending upon what part of the body is most exposed.

Glucose metabolism and cell phones (Volkow et al., 2011)



National Toxicology Program (NTP) and Ramizzini Institute Reports

- The NTP project was a 2-year exposure of rats to cell phone intensities of RF-EMFs.
- "Following exposure to GSM- or CDMA-modulated cell phone RFR there were increases in the incidence of malignant Schwannoma of the heart….Several other weaker responses were observed with both modulations, including malignant glioma in the brain, adenomas in the pituitary gland… and pheochromocytomas of the adrenal cortex,"
- "A significant increase in DNA damage was observed in hippocampus cells of male rats exposed to CDMA modulation."
- The Ramazzini Institute study was similar but at an intensity like that from cell towers. They founds essentially the same cancers as the NTP study but at lower levels of exposure.

Other Health Effects

- Reproductive harm: Reduced sperm counts and infertility in men, some increase in spontaneous abortion and premature birth in women.
- Effects on brain function: Reduced learning ability, especially in children. Impaired memory in adults. This is a special problem in wireless computer classrooms in schools.
- Electro-hypersensitivity: In some people development of headaches, insomnia, heart palpitations, tinnitus and a general feeling of ill health.

RFR and Male Fertility

- In a meta-analysis for 185 studies of 42,935 men, there has been a 50-60% decline in sperm counts in between 1973 and 2011 (Levine et al., 2017).
- Isolated human sperm exposed to 1.8 GHz RFR show reduced motility and vitality, mitochondrial generation of reactive oxygen species and DNA fragmentation (DeIullis et al., 2009). Sperm placed near a wireless laptop for four hours showed DNA fragmentation and reduced motility (Avendano et al., 2012)
- There was a significant decrease in sperm counts in men carrying their mobile phone in their trouser related to time spend sending or receiving calls (Al-Bayyari, 2017)

Symptoms of Electro-Hypersensitivity (EHS)

- EHS is one of a series of syndromes, called “ideopathic environmental intolerance” or “medically unexplained symptoms” characterized by fatigue, headache, weakness, memory impairment, sleep disturbances and a general feeling of ill health.
- EHS frequently co-exists with chronic fatigue syndrome, multiple chemical sensitivity, Gulf War Illness, fibromyalgia and several other less common diseases.
- The cause of each of these disorders is unknown, but at least for some of them there is an initial triggering event.

Historical Perspectives on EHS

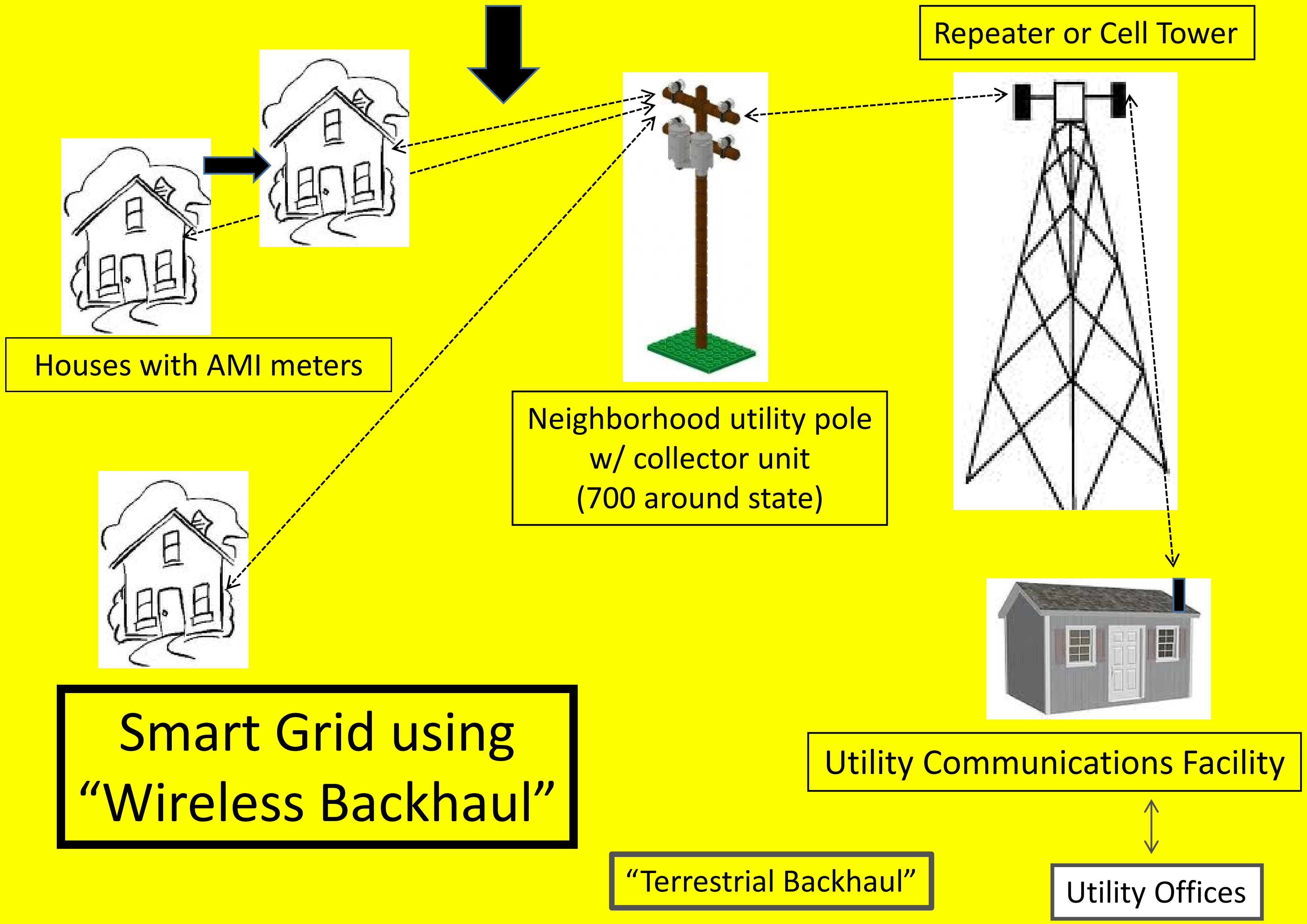
- Western countries have considered that there can be no adverse biological effects of electromagnetic fields (EMFs), including radiofrequency (RF) fields, that are not mediated by tissue heating.
- The Soviets, on the other hand, reported years ago that individuals experienced headache, fatigue, difficulty in concentration, depression, emotional instability and irritability when exposed to RF fields at intensities much lower than those causing measureable tissue heating.

Health Effects of RF Radiation

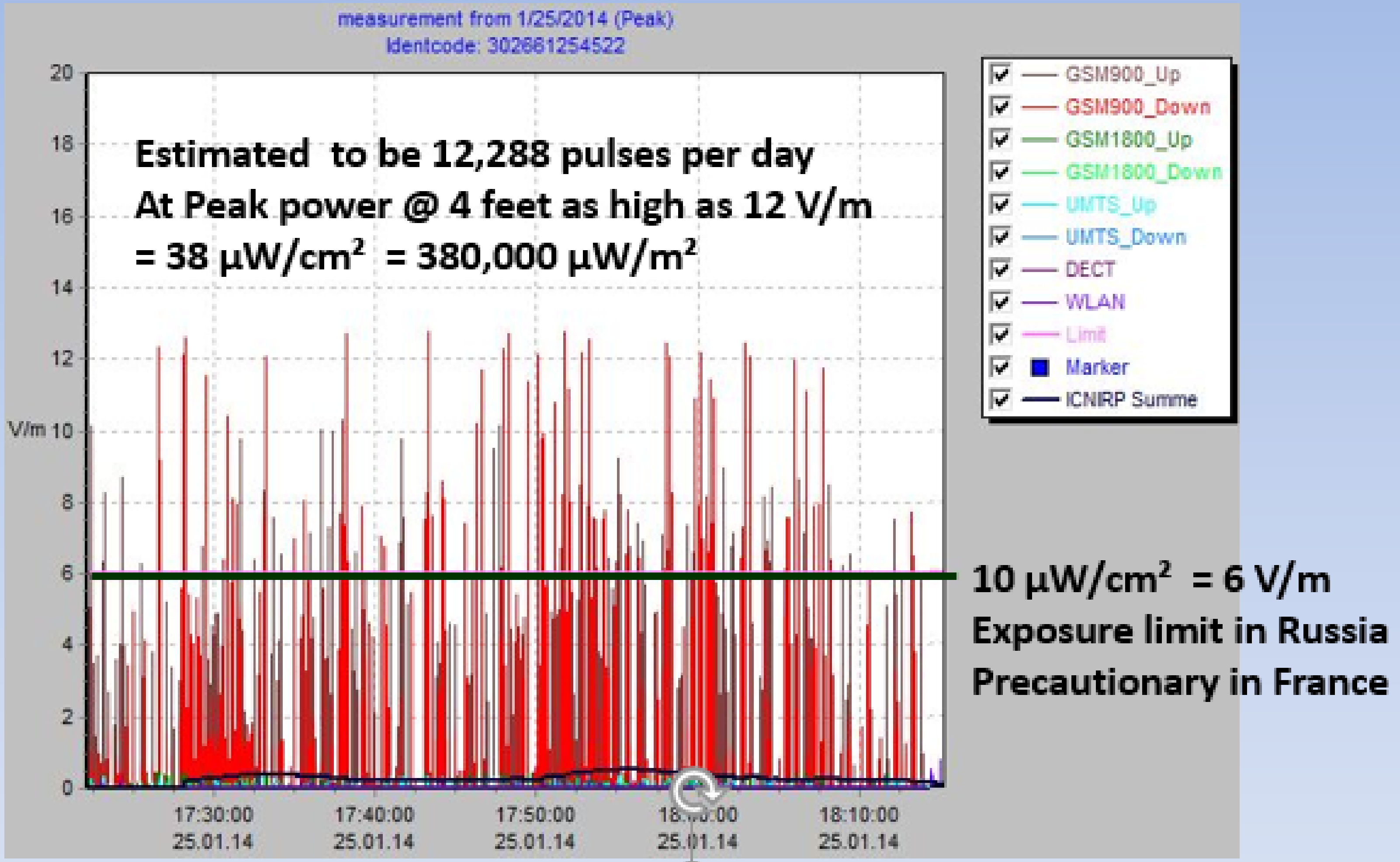
- Beginning in 1953 the US Embassy in Moscow was irradiated with microwaves at up to 0.18 W/m^2 and frequencies from 0.6 to 9.5 GHz.
- While no elevations of cancer were found, many people developed “microwave sickness”, consisting of headaches, insomnia, irritability and emotional lability.
- “Microwave sickness” is EHS!

Reports of Excessive Exposure to Radar

- Forman et al. (JOM 24: 932: 1982) reported on two men accidentally exposed to radar microwaves. Both exhibited symptoms of headaches, insomnia, irritability and emotional lability even after a 12-month follow-up.
- Schilling (OEM 54: 281: 1997) reported on three men acutely exposed to 785 MHz RF who immediately developed EHS symptoms that lasted over a 3-year follow-up. Later (OM 50: 49: 2000) he reported on six antenna engineers acutely exposed in two separate incidents. Four developed EHS with no improvement over 3-4 years follow-up. Headache, loss of stamina, malaise and lassitude were the major symptoms.


Repeater or Cell Tower
Houses with AMI meters
Neighborhood utility pole
w/ collector unit
(700 around state)
Smart Grid using
“Wireless Backhaul”
Utility Communications Facility
“Terrestrial Backhaul”
Utility Offices

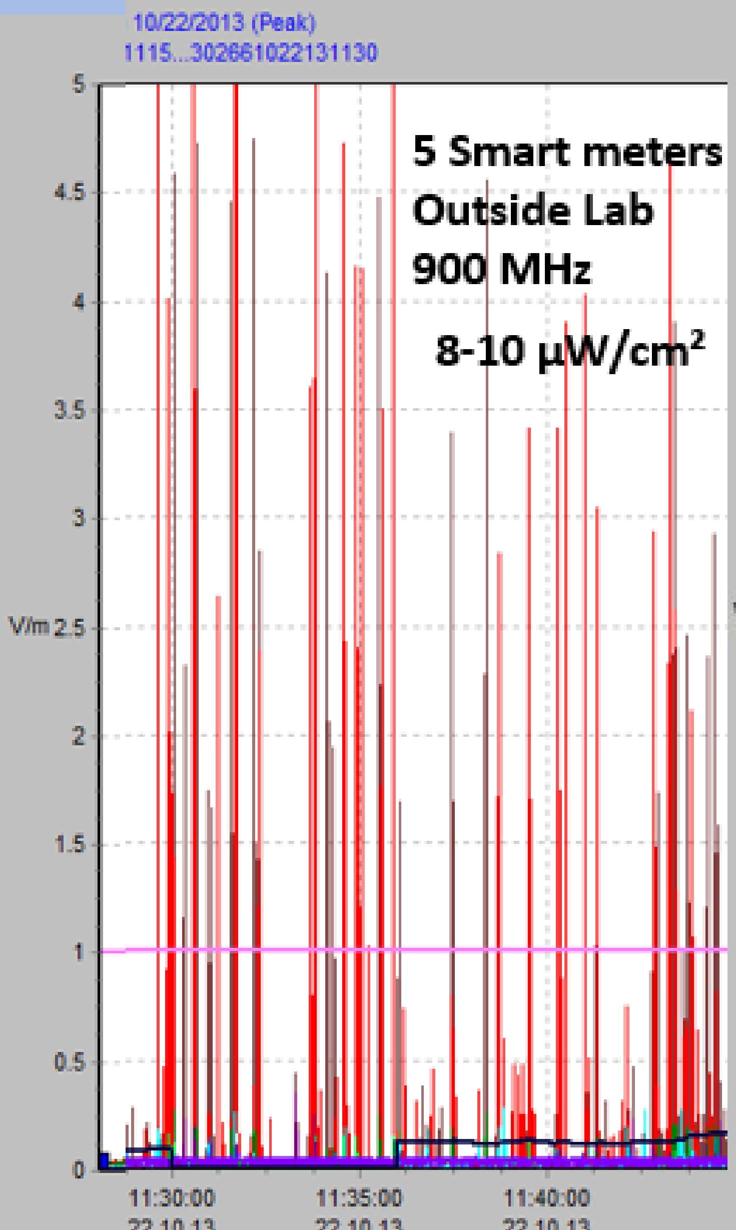
Daily Pulses Generated by Smart Meter

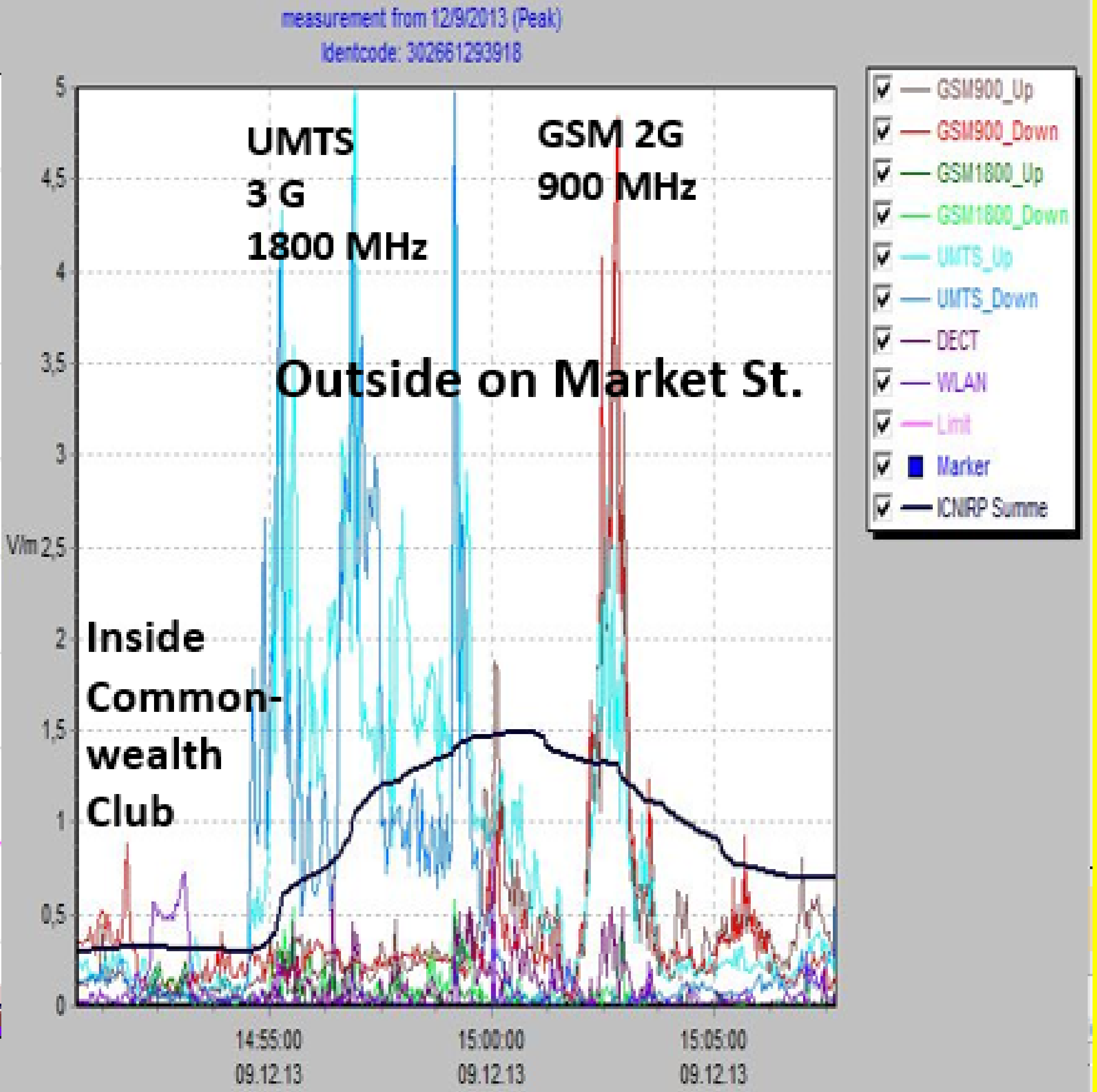


- Depends on Duty Cycle and other meters in the Mesh network
- Data from 5 meters shows 340 pulses in 40 minutes =12,288/day
- Emissions are brief (5 msec), but fast pulses affect nervous system

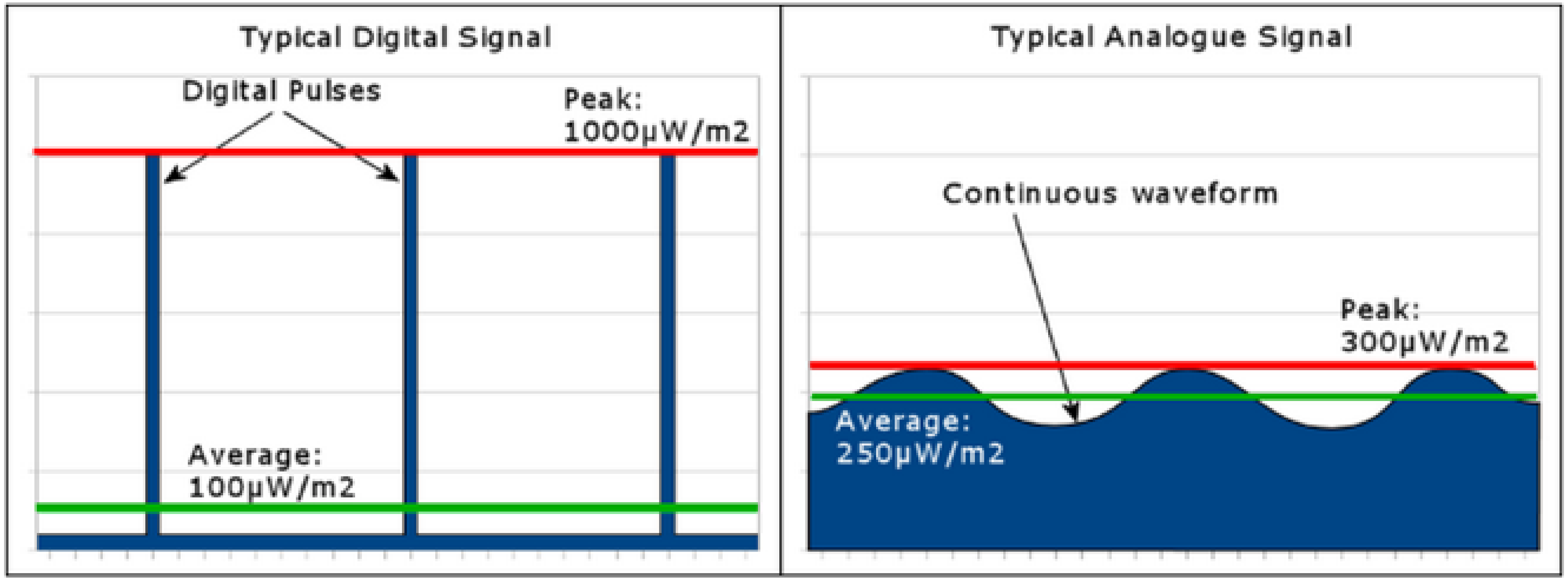
Smart Meters @ 8 feet : Market St. San Francisco

15 minutes on Oct 22, 2013 15 minutes on Dec 9, 2013





Peak Levels in Digital Signals are Higher



- Smart Meters send out high intensity short pulses
- Peak pulse intensities trigger biological systems more powerfully

EHS: Somatic Response is not Conscious

Int J Neurosci. 2011 Jul 28. [Epub ahead of print]

ELECTROMAGNETIC HYPERSENSITIVITY: EVIDENCE FOR A NOVEL NEUROLOGICAL SYNDROME.

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Abstract

ABSTRACT Objective: We sought direct evidence that acute exposure to environmental-strength electromagnetic fields could induce somatic reactions (EMF hypersensitivity). Methods: The subject, a female physician self-diagnosed with EMF hypersensitivity, was exposed to an average (over the head) 60-Hz electric field of 300 V/m (comparable to typical environmental-strength EMFs) during controlled provocation and behavioral studies. Results: In a double-blinded EMF provocation procedure specifically designed to minimize unintentional sensory cues, the subject developed temporal pain, headache, muscle-twitching, and skipped heartbeats within 100 s after initiation of EMF exposure ($P < 0.05$). The symptoms were caused primarily by field transitions (off-on, on-off) rather than the presence of the field, as assessed by comparing the frequency and severity of the effects of pulsed and continuous fields in relation to sham exposure. The subject had no conscious perception of the field as judged by her inability to report its presence more often than in the sham control. Discussion: The subject demonstrated statistically reliable somatic reactions in response to exposure to subliminal EMFs under conditions that reasonably excluded a causative role for psychological processes. Conclusion: EMF hypersensitivity can occur as a bona fide environmentally-inducible neurological syndrome.

PMID: 21793784 [PubMed - as supplied by publisher]

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American Academy of Environmental Medicine Recommendations Regarding Electromagnetic and Radiofrequency Exposure

- The AAEM recommends that:
- Patients with (certain) medical conditions and disabilities be accommodated to protect their health.
- No Smart Meters be on these patients' homes;
- Smart Meters be removed within a reasonable distance of patients' homes depending on the patients' perception and/or symptoms;

2011 Survey after Smart Meters Installation

- 443 respondents to a survey, 93% over 40 years of age
- 78% from California, 73% women, 49% reported EHS
- 76% had meters installed neighborhood > 6 months, 41% had meters installed in their homes

- Complaints:
  - Sleep Issues = 49%
  - Stress, anxiety, irritability = 43%
  - Headaches = 40%
  - Ringing in Ears = 38%
  - Heart Problems / palpitations = 26%

- Source: Halteman, Ed (2011) Wireless Utility Meter Safety Impacts Survey. Available at http://emfsafetynetwork.org/wp-content/uploads/2011/09/Wireless-Utility-Meter-Safety-Impacts-Survey-Results-Final.pdf

Advanced Metering Infrastructure (AMI)

Customers will gain control of their water usage via an information portal. AMI technology improves customer experience by providing access to near real-time water-usage information and helping to quickly recognize potential leaks and other home plumbing issues, which can significantly reduce bills and save money. An additional benefit is a decrease of WSSC Water's carbon footprint by reducing the number of trucks that we have on the road.

Conclusions

- EHS is real, but not everyone is electrosensitive.   There is something about the signals from AMI smart meters that makes them particularly provocative, probably the very rapid rise and fall of the signals.
- EHS is related to other disease syndromes characterized by similar symptoms. Much more study is needed to determine what are the triggering events and especially what are the mechanisms of action.
- AMI meters benefit the utility but not the consumer.
- Individuals who become ill from AMI meters placed on their home should have the ability to “opt-out” because they are dangerous to the health of those who are sensitive to RF signals.

20 October 2020

WSSC Water:

Thank you for the opportunity to present to the WSSC Water committee, and respond to the report by Leeka Kheifets, PhD on potential impacts on human health of advanced metering infrastructure.

I am a public health physician who serves as director of the Institute for Health and the Environment, a Collaborating Center of the World Health Organization, as well as a professor of Environmental Health Sciences at the University at Albany School of Public Health. I previously served as Director of the Wadsworth Center of the New York State Department of Health, and as Dean of the University at Albany School of Public Health. I received my medical degree from Harvard Medical School, have more than 450 peer-reviewed publications, six books and 50 reviews and book chapters. I am also co-editor of the "BioInitiative Report," first published in 2007, a comprehensive review of the adverse health effects of radiofrequency electromagnetic fields.

Smart AMI meters and cell phones occupy similar frequency bands of the electromagnetic spectrum, meaning that cell phone research can apply to smart meter radiofrequency radiation (RFR). Smart meter RFR consists of frequent, very intense but very brief pulses throughout the day. Because smart meter exposure over a 24 hour period can be very prolonged (pulses can average 9,600 times a day), and because there is building evidence that the sharp, high intensity pulses are particularly harmful, the cell phone study findings are applicable when discussing adverse health impacts from smart meters.

While the strongest evidence for hazards coming from RFR is for cancer, there is a growing body of evidence showing other effects including impacts to the brain and reproductive system. In addition, some people develop a condition called electro-hypersensitivity (EHS). These individuals respond to being in the presence of RFR with a variety of symptoms, including headache, fatigue, memory loss, ringing in the ears, "brain fog" and burning, tingling and itchy skin. Some reports indicate that up to three percent of the population may develop these symptoms, and that exposure to smart meters is a trigger for development of EHS.

In short:

- Smart meters operate with much more frequent pulses than cell phones, increasing the potential for adverse health impacts.
- Smart meter pulses can average 9,600 times a day, and up to 190,000 signals a day. Cell phones only pulse when they are on.

- Cell phone RFR is concentrated, affecting the head or the area where the phone is stored, whereas smart meter RFR affects the entire body day and night.
- An individual can choose whether or not to use a cell phone and for what period of time. When smart meters are placed on a home the occupants have no option but to be continuously exposed to RFR. Even if they opt-out neighbors will have transmitting meters elevating the ambient levels in the neighborhood.

I am aware that the WSSC received a report entitled "On potential impacts on human health of advanced metering infrastructure" and I strongly disagree with the conclusion stated at the WSSC Commission meeting on February 19, 2020 at 3:29:40 that "…with smart meters, the exposures are so low that...concern is unwarranted." The research findings by independent scientists point to a clearer relationship between RFR and health effects than industry-funded studies and independent scientists believe that a network of radiofrequency radiation (RFR) generating meters in a neighborhood poses numerous health and environmental issues warranting attention. It does not make sense to dismiss smart meter exposures as "low" because this is a new network of thousands of RFR transmitting devices. Governments should be reducing RFR exposures, not increasing them.

The adverse health impacts of low intensity RFR are real, significant, and for some people debilitating. I want to stress four fundamentals as the WSSC proceeds to consider wireless meters:

- The Federal Communication Commission's "safety" standards do not apply to protection from biological effects of long-term exposure to low intensity RFR.
- There is no safe level of exposure established for RFR.
- People around the world are suffering from low intensity RFR exposure, being at increased risk of developing cancer, electrical sensitivity as well as other medical conditions.
- The Federal Communication Commission's "safety" standards do not apply to flora and fauna and thus the trees and wildlife exposed to the radiofrequency radiation are without any federal regulations or protections.

Published research documents that radiofrequency radiation is a human carcinogen.

Page 15 of the WSSC Report states "*International Agency for Research on Cancer has classified RF as a 'possible human carcinogen' (Group 2B) based on 'limited evidence' from both human and animal studies (Ref.: 15) the weight of evidence has not risen to a level that would change the basis for RF exposure limits.*"

As of 2020, several expert independent scientists have published their evaluation that the scientific evidence has increased and radiofrequency radiation should be classified as proven human carcinogen (Belpomme et al., 2018; Miller et al., 2018; Hardell and Carlberg, 2019).

The 2011 World Health Organization International Agency for Research on Cancer (WHO/IARC) classification of RF-EMFs as a "possible" human carcinogen was based primarily on evidence from human studies 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 IARC rating was not at "probable" or "known" was the lack of clear evidence from animal studies for exposure leading to cancer.

In 2018, the US National Institute of Environmental Health Sciences National Toxicology Program's (NTP) Studies of Cell Phone Radiation released their findings that chronic exposure to RFR was associated with "clear evidence" of cancer in RFR-exposed male rats (NTP, 2018). In addition, exposed animals had significantly more DNA damage, heart damage and low birth weight (Smith Roe et al., 2020). Similar results in rats have been reported in an independent large scale animal study from the Ramazzini Institute with levels of exposure far lower than the NTP study and 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).

Due to the large scale animal studies as well as additional published research since 2011, the WHO/IARC advisory group published their recommendation that IARC should evaluate non-ionizing radiofrequency radiation as a "high priority" in the next five years. Documentation can be found at IARC Monographs on the Identification of Carcinogenic Hazards to Humans Report of the Advisory Group to Recommend Priorities for the IARC Monographs during 2020–2024 on page 148.

Published research documents adverse effects at levels well below FCC limits.

Page 4 of the WSSC Report states *"The exposures to RF from smart meter are neither long enough nor strong enough to approach the safety standards set by the Federal Communications Commission (FCC) and other bodies."*

First, FCC limits are not protective and thus any comparison to these limits has no relevance to impacts on health and the environment. The current 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 (Bandara and Carpenter, 2018).

"Numerous recent scientific publications have shown that EMF affects living organisms at levels well below most international and national guidelines. Effects include increased cancer risk, cellular stress, increase in harmful free radicals, genetic damage, structural and functional changes of the reproductive system, learning and memory deficits, neurological disorders, and negative impacts on general well-being in humans. Damage goes well beyond the human race, as there is growing evidence of harmful effects to both plant and animal life" (Kelley et al., 2015).

The various agencies setting safety standards including the FCC have failed to impose sufficient guidelines to protect the general public, particularly children who are more vulnerable to the effects of EMF. Reliance on FCC limits does not ensure safety.

Published research documents that even low levels of radiofrequency radiation have adverse impacts.

Page 3 of the WSSC Report states *"Because Smart meters are not used in close proximity to human body (unlike cell phones, tablets, computers and even WIFI) and because they transmit relatively infrequently their exposure levels are very low and far below U.S. and international exposure limits."*

Wireless smart meters typically produce atypical, relatively potent and very short pulsed RF/microwaves. Technical spec sheets on AMI water meters show these types of meters transmit very frequently - with a mobile message every 14 seconds at 100 mW and every 7 1⁄2 minutes at 1 Watt (See Neptune R900i Spec Sheet). Constant emissions is the only way for meters to transmit information wirelessly in "real time." Smart utility meters transmit very high intensity but short pulses. Even if the duration of the pulse is short, the pulse can be intense and research has found that low level exposures have biological effects (Bioinitiative Report Charts). In addition, the resulting biological effects from an exposure may be due both to the pulsed and polarized characteristics of man-made EMFs emitted wireless technologies which contrast to the non-polarized natural electromagnetic fields humans have been exposed to for decades (Belyaev, 2015, Panagopoulos et al., 2015).

Second, water utility meters are both inside homes as well as outside homes on walls near living spaces for families. The WSSC report states that "about 60% of WSSC water meters are located inside the basement of homes and 40% are located outside the home at the property line." Hence, there are opportunities for people to be in close proximity to the meters and receive intense exposures. Equally important is that people will be exposed day and night.

Hundreds of scientists are calling on policymakers to reduce RF levels to protect the public and the environment and identify smart meters as a source of radiofrequency radiation exposure.

The WSSC Report page 21 states that *"A group of scientists published an appeal in which they question adequacy of existing guidelines for RF from variety of devices, including smart meters...most official organizations do not share this concern."*

The International EMF Scientist Appeal signed by over 250 scientists states "Based upon peer-reviewed, published research, we have serious concerns regarding the ubiquitous and increasing exposure to EMF generated by electric and wireless devices. These include–but are not limited to–radiofrequency radiation (RFR) emitting devices, such as cellular and cordless phones and their base stations, Wi-Fi, broadcast antennas, smart meters…"

There are numerous medical organizations recommending that exposure to radiofrequency be reduced and they include American Academy of Pediatrics, ANSES, France's National Agency for Food, Environmental and Occupational Health Safety, Turin Medical Association of Italy, The American Academy of Environmental Medicine, Swiss Physicians Association of Doctors for Environmental Protection, African Cancer Organisation, The Cyprus National Committee on Environment and Child Health, Austrian Medical Association, Athens Medical Association, Canadian Parliament House Standing Committee on Health.

For anyone to downplay the exposure from smart meters as contributing just a "low" level downplays the actuality that a person's total exposure comes from a combination of sources inside and outside the home. Smart meters would contribute to this total daily exposure. The toxic metal lead is not known to be safe at any level and companies worked for years to downplay the science showing harm. It makes sense to reduce exposure as much as possible.

Children and pregnant women are most vulnerable to radiofrequency radiation.

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 in abnormalities later. 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. 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 greater cumulative exposure than adults (Belpomme et. al, 2018).

Research on animals (Bas et al., 2009; Deshmukh et al., 2015; Shahin et al., 2017; Megha et al., 2015; Aldad et al., 2012; Zhang et al., 2015) shows impacts from RFR to the brain such as alterations in neurodevelopment and behavior of offspring, impaired learning and spatial memory, a deleterious impact on hippocampal, pyramidal or cortical neurons and induced markers of oxidative stress and inflammation in the brain. Human data is consistent with these animal studies as they have found higher cell phone radiation associated with behavioral problems and memory damage (Divan et al., 2012; Birks et al. 2017; Foerster et. al., 2018).

The research showing impacts from radiofrequency on the brain again highlights the importance of reducing exposure to children and pregnant women. There is no safe level of radiofrequency radiation identified.

Radiofrequency radiation has been found to interact with other toxic exposures and have synergistic reactions.

Early life exposure to lead has long been known to harm children and impact their ability to pay attention. 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 indicate that EMFs can have synergistic actions with other environmental contaminants known to cause a reduction in intelligence quotient (IQ).

In addition, replicated results from animal studies show co-carcinogenic and tumor promoting effects from RF-EMF when RF is combined with a known carcinogen (Tillmann et al., 2010; Lerchl et al., 2015). The studies used a very low level of radiofrequency radiation yet found increases in tumors from the combined exposures.

Industry influence is impacting the science on radiofrequency radiation.

The evaluation of RFR health risks is often ignored by government authorities. Conflicts of interest and ties to the industry seem to have contributed to the biased reports by various organizations (Hardell,2007; 2017; Hardell and Carlberg, 2020; Hardell and Nyberg, 2020; Harvard University Press, 2018; Ledford, 2010; Starkey, 2016). The lack of proper unbiased risk evaluation of radiofrequency radiation places populations at risk. I published an article (Carpenter, 2019) on lower frequency electromagnetic radiation and found that when one allows for bias reflected in source of funding, the scientific evidence that magnetic fields increase risk of cancer is neither inconsistent nor inconclusive. It is clear when one excludes biased reports from individuals and organizations that have conflicts of interest that the adverse health effects resulting from exposure to RFR are well-documented, are found consistently in studies from around the world, and require that government and regulatory agencies take action to protect the public from excessive exposure to RFR.

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Environmental Pollution 242 (2018) 643–658

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

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

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A R T I C L E I N F O

Article history:
Received 6 April 2018
Received in revised form
31 May 2018
Accepted 4 July 2018
Available online 6 July 2018

A B S T R A C T

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.

☆ This paper has been recommended for acceptance by Payam Dadvand.

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https://doi.org/10.1016/j.envpol.2018.07.019
0269-7491/© 2018 Published by Elsevier Ltd.

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

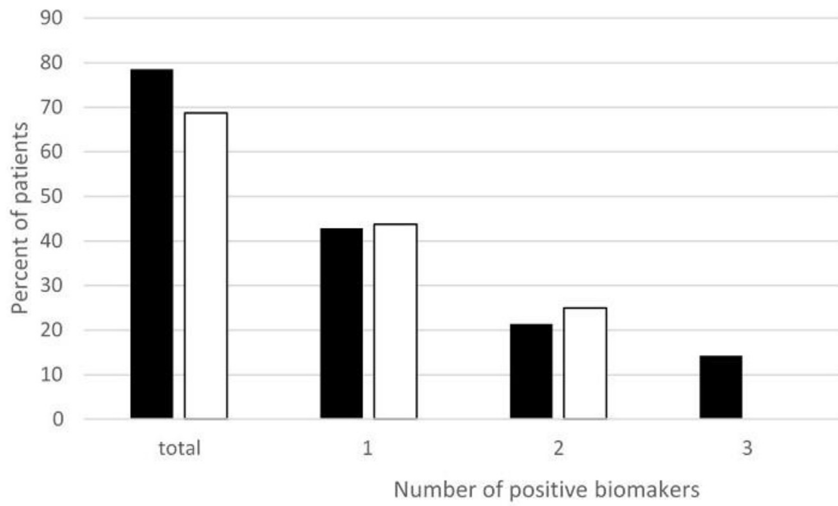

Fig. 1. Percentage of EHS self-reporting patients having positive TBARs, GSSG and/or NTT oxidative stress biomarkers measured in the peripheral blood. "Positive" biomarkers correspond to marker levels above the upper normal limit; "total" corresponds to the patients with one or more positive biomarker 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 electro-hypersensitivity*

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

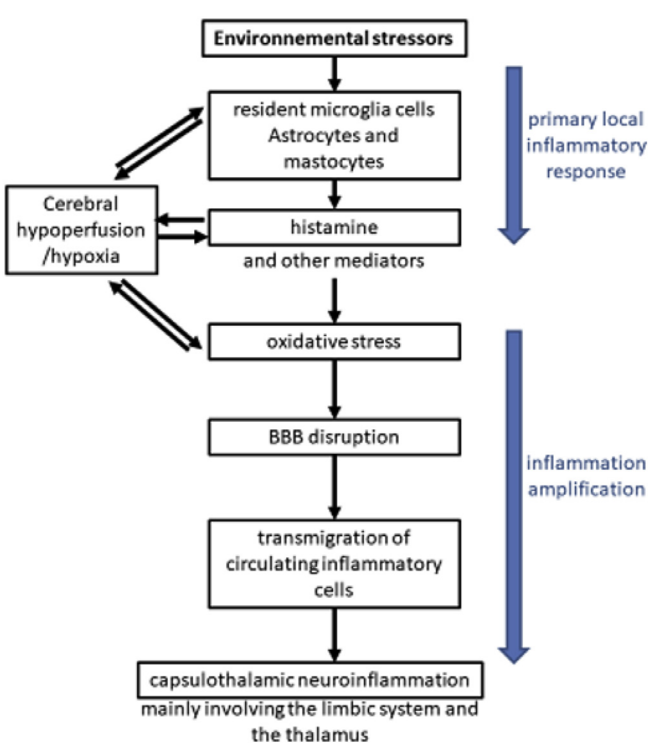

Fig. 2. Hypothetical EHS/MCS common etiopathogenic model based on neuroinflammation and oxidative/nitrosative stress-induced blood brain barrier disruption (Belpomme et al., 2015).

variables affecting cellular responses to EMFs (Liburdy and Vanek, 1987; Sannino et al., 2011).

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 arithmetric 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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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

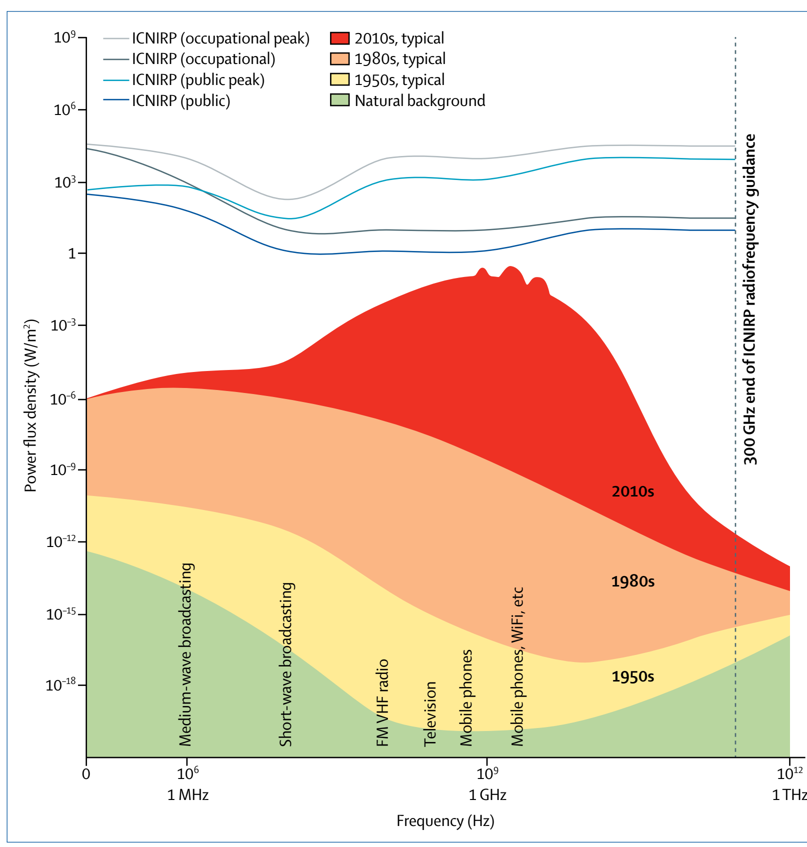

***Figure:* Typical maximum daily exposure to radiofrequency electromagnetic radiation from man-made and natural power flux densities in comparison with International Commission on Non-Ionizing Radiation Protection safety guidelines[1]**

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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We declare no competing interests. We thank Alasdair Philips for assistance with the figure and Victor Leach and Steve Weller for assistance with the ORSAA Database, which has enabled our overview of the scientific evidence in this area of research.

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