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Review Article

Electromagnetic Fields: Insight into Sources, and Their Effects on Vital Organs and the Risk of Cancer

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Abstract: ***Background*:** Electromagnetic radiation has become an extensive new pollution source in modern civilization. Therefore, the biological effects of electromagnetic radiation have attracted considerable attention worldwide. ***Objectives*:** The current review was aimed to highlight on sources of electromagnetic fields and their effects on vital organs and the risk of cancer. Electromagnetic sources can be classified into natural electromagnetic sources (sun, some distant stars, atmospheric discharges like thunder, or human body) and unnatural or human made sources (printers, vacuum cleaners, cellular phones, hair dryers, refrigerators, washing machines, kettles microwaves, cables that carry electrical currents, television and computers, electrical home gadgets, radio and television base stations, mobile phone base stations and phone equipment), home wiring airport, and transformers. Electromagnetic fields (EMFs) are electromagnetic waves less than 300 GHz, that are divided into extremely low frequencies (ELFs; 3–3,000 Hz), involving high-voltage transmission lines and in-house wiring; and radiofrequencies (RFs; 30 kHz to 300 GHz), involving mobile phones, smart devices, base stations, WiFi, and 5G technologies. Cell phone technology is an integral part of everyday life and its use is not only restricted to voice conversations but also conveying news, high-resolution pictures, and the internet. Exposure to electromagnetic fields might produce oxidative stress, sperm damage, DNA damage, changes in the chromatin conformation, formation of micronucleus in different cell types, gene expression, enzyme activity, and changes in the structure and function of cell membrane, stimulated an increase in apoptosis and biosynthesis of plasma metallothionein and corticosterone. It causes headaches, chronic fatigue, heart problems, stress, nausea, chest pain, gastrointestinal issues, pain in the muscles and joints, sweating, neurocognitive disturbances, eye burning, nose, ear, and throat issues, bad effects on reproductive, central nervous, endocrine, cardiovascular, and immune systems. Also, it increases anxiety-related behavior; spatial memory, and learning deficits in male mice offspring, decreased thermal pain perception, induced a sleep disturbance, latency, and day dysfunction especially in females, a change in memory performance, damage to the lens epithelial cells of rabbits after 8 hours of exposure to microwave radiation, produced lens opacity in rats, which is linked to the production of cataracts, and derangement of chicken embryo retinal differentiation. There are a relationship between exposure to electromagnetic fields and the increased incidence of the occurrence of some tumors types, particularly brain cancer and leukemia. EMFs induce damage of tissues by increasing free radicals and changing the antioxidant defense systems of tissues, eventually leading to oxidative stress which leads to behavioral, histopathological and biochemical alterations. Exposure to radar, which uses RF fields above 6 GHz similar to 5 G causes effects on production of cancer at different sites, and other diseases. The possible mechanism proposed of how EMFs lead to cancer is the impact of EMFs on free radical combination rates in certain enzymes, such as coenzyme B_{12}-dependent ethanolamine ammonia lyase. The enzyme reaction rate may be amplified by a factor of up to 100. A case-control studies found an increased risk of gliomas, acoustic neuromas, and temporal lobe tumours in users with highest self-reported cell phone use. Exposure of experimental animals to microwave radiation caused a decrease in learning and memory ability, abnormal hippocampal morphology and abnormal Electroencephalogram. Also, it could lead to a decrease in norepinephrine and epinephrine contents in the brain, leading to neurotransmitter production disorders. ***Conclusion*:** It can be concluded that electromagnetic sources classified into natural electromagnetic and human made sources. EMFs) are electromagnetic

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waves less than 300 GHz are divided into extremely low frequencies and radiofrequencies. Exposure to electromagnetic fields might produce oxidative stress, which leads to histopathological and biochemical alterations in different body organs and increased risk of gliomas, acoustic neuromas, and temporal lobe tumours in users with highest self-reported cell phone use. Further studies are needed to confirm these effects in human and experimental animals.

Keywords: Electromagnetic fields**,** Sources of EMFs, Wireless Communication, Cell phones, Health hazards, Risk of Cancer.

INTRODUCTION

In the past 30 years, technical achievements based on electromagnetism have been widely used in various fields pertaining to human production and life (Hu *et al.*, 2021). There is an electric field around every electrical installation caused by the electric charge transport due to the presence of an electric potential difference. The intensity of the created field depends on the voltage. Indeed, the magnetic field is the result of the current produced by charge movement (Baptiste, 2001, Salah *et al.*, 2017). Cell phones have become a vital part of everyday life. It creates an EMF around them when in use, thus increasing the electromagnetic contamination (Azab *et al.*, 2018). Therefore, electromagnetic fields are the result of the combination of both electric and magnetic fields which move together at the speed of light. It is characterized by its frequency and its wavelength (Hée *et al.*, 2002, Salah *et al.*, 2017). The electromagnetic radiation has become a substantial new pollution source in modern civilization. The biological effects of electromagnetic radiation have attracted considerable attention worldwide (Hu *et al.*, 2021). A recent study mentioned that exposure to electromagnetic fields might produce a variety of adverse effects on human health as headaches, chronic fatigue, heart problems, stress, nausea, chest pain, and also some bad effects on central nervous, endocrine, and immune systems (Jbireal *et al.*, 2018). Lai H, and Singh, 1996, Lixia *et al.*, 2006, and Zhao *et al.*, 2007 reported that exposure to electromagnetic field resulted in DNA damage, changes in the chromatin conformation, formation of micronucleus in different cell types, gene expression, enzyme activity, and changes in the structure and function of cell membrane (Savitz, 1995, Lewy *et al.*, 2003, Yokus *et al.*, 2005). Also, subacute exposure to static electromagnetic fields stimulated an increase in apoptosis and biosynthesis of plasma metallothionein and corticosterone in female rats, that may be linked to oxidative stress (Chater *et al.* 2005). Wertheimer *et al.*, 1995, Aldrich *et al.*, 2001 recorded that a relationship between exposure to electromagnetic fields and the increased incidence of the occurrence of some tumors types, particularly brain cancer and leukemia.

The electromagnetic spectrum

Electromagnetic radiation is generated from natural environments such as the solar energy and geomagnetic field or from manmade sources. With scientific and technological advancements, our everyday environments are filled with various manmade electromagnetic fields (EMFs). EMFs are invisible and generated from transmission towers, electrical lines, telecommunications, mobile phones, home appliances, base stations, and WiFi. An increasing number of children use iPads and computers for entertainment, school, and social activities. Even infants can be exposed to EMFs in the residential environment or by the direct use of electronic devices (Figure 1) (Moon, 2020).

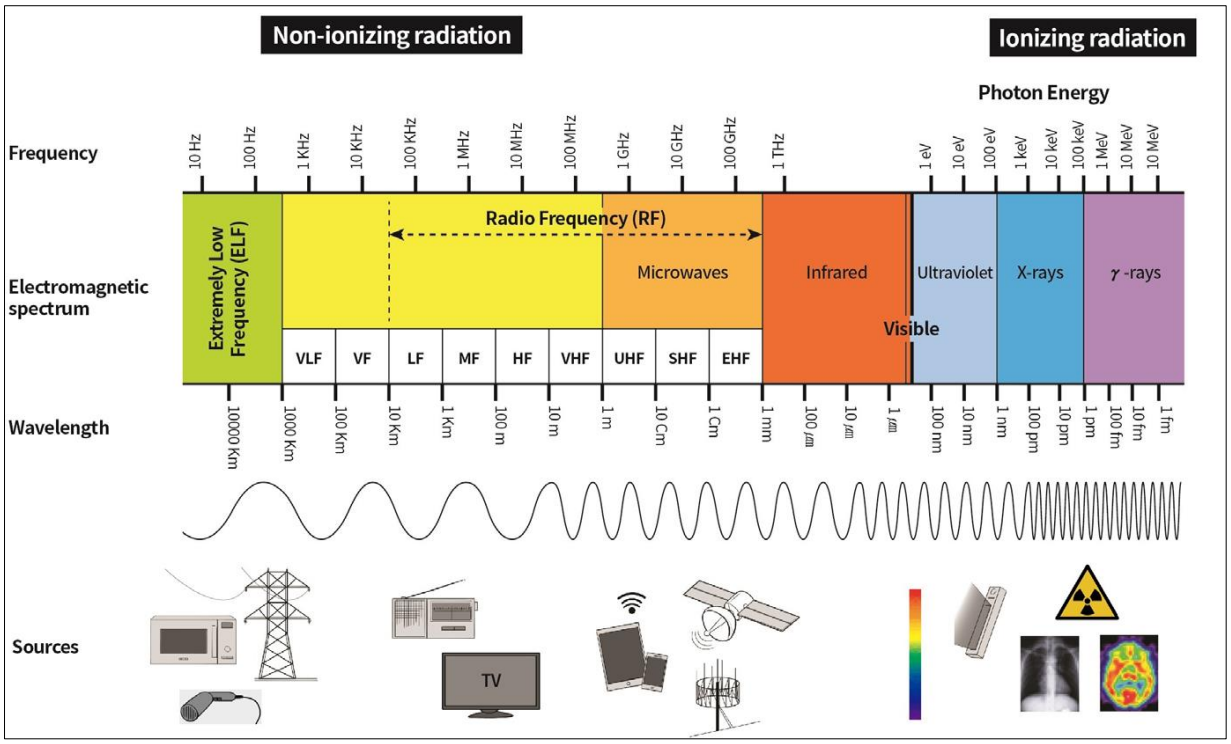

Figure 1: The electromagnetic spectrum. Frequencies (expressed by hertz, Hz) increase from left to right, while wavelengths decrease from right to left. Ionizing radiations are x-rays and γ-rays. EHF, extremely high frequency; HF, high frequency; LF, low frequency; MF, medium frequency; SHF, super-high frequency; VF, voice frequency; VHF, very high frequency; VLF, very low frequency; UHF, ultra-high frequency (Moon, 2020)

Non-ionizing radiation covers a broad spectrum of energy frequencies, which includes RF. RF is part of the EM spectrum and spans 3 kHz to 300 GHz. RF is both naturally-occurring and generated from human activities, and has been used in many applications for communications globally for decades. Examples include television and radio broadcast, WiFi, cordless telephones, cell phones, smart meters, and satellite communication. Microwave ovens also use RF to heat objects. Though existing and planned telecommunications networks including 5G operate within the EM spectrum, more higher-frequency bands will come into use with the roll out of 5G technology, which will enable increased mobile data capacity, decreased latency, and the "internet of things", which refers to devices that autonomously use data (e.g., autonomous vehicles). 5G will make greater use of RF frequencies from 600 MHz to around 30 GHz, and possibly higher, in what has been referred to as the "millimetre band" or "millimetre wave" (MMB or MMW) range (which extends to 300 GHz) (Innovation, Science and Economic Development Canada, 2018, Health Canada, 2019).

Classification of Electromagnetic sources

Electromagnetic sources can be classified into natural electromagnetic sources (sun, some distant stars, atmospheric discharges like thunder, or human body) and unnatural or human made sources (printers, vacuum cleaners, cellular phones, hair dryers, refrigerators, washing machines, kettles microwaves, cables that carry electrical currents, television and computers, electrical home gadgets, radio and television base stations, mobile phone base stations and phone equipment), home wiring airport, and transformers (Ebrahim *et al.*, 2016). The artificial sources of electromagnetic radiation have risen tremendously because of the ongoing need for electricity, telecommunications, and electronic devices. New technologies that use the spectrum of high-frequency emissions are incorporated into many aspects of telecommunications. Consequently, there is a lot of interest in the possible effects of the radiation emitted from telecom machines such as hand phones, base stations, and transmitters (Pourlis, 2009, Azab *et al.*, 2018). Cell phone technology is an integral part of everyday life and its use is not only restricted to voice conversations but also conveying news, high-resolution pictures, and the internet. However, these technological advances are accompanied by a progressive boost in the intensity and frequency of the emitted electromagnetic waves without considering their health consequences (Hamada *et al.*, 2011, Azab *et al.*, 2018). Most 3G phones use the Universal Mobile Telecommunications System's (UMTS), W-CDMA2 air interface standard, which operates at a higher frequency range of 1900–2170 MHz and is without periodic pulsed modulation content. There is evidence that the frequency components may be very important for mobile phone-related biological effects (Kesari *et al.*, 2013, Kesari *et al.*, 2014).

Electromagnetic fields (EMFs) are electromagnetic waves less than 300 GHz. EMF exposure is divided into 2 categories: extremely low frequencies (ELFs; 3–3,000 Hz), involving high-voltage transmission lines and in-house wiring; and radiofrequencies (RFs; 30 kHz to 300 GHz), involving mobile phones, smart devices, base stations, WiFi, and 5G technologies ((IARC, 2002, Kheifets *et al.*, 2005, IARC, 2013, Moon, 2020). The 4G/Long-Term Evolution (LTE) offers a minimum signal delay of 20 ms mainly designed for the internet which is required for real-time integration of sensor data. Also, Wi-Fi solutions are an alternative, but they can be interrupted by other users at any time due to unprotected radio bands (Sauter, 2018, Georgiou *et al.*, 2021). The new 5G telecommunication standard offers high bandwidths as compared to the current mobile transmission standard 4G/LTE: 5G is a 100 times higher data transmission rate (up to 10GB/s), and, at the same time, an extremely low latency time (<1ms), and 1000 times higher capacity (bandwidth) with a high quality of service which is almost equal to the zero data response time in the real world (Andrews *et al.*, 2014, Georgiou *et al.*, 2021). Millimeter wave telecommunication is such an advantageous technology for 5G networks because it allows extremely high data transfer speeds (several gigabits per second). However, a large number of small cells with limited radius deployment must be used to achieve seamless and efficient coverage and form a 5G ultra-dense cellular network. The cells may be of different sizes, and they are classified as Femtocells, Pico-cells or Microcells. The massive multi-input, multi-output is an evolving technology capable to transmit multiple data beams at a time, thus increasing the throughput and spectrum effectiveness in both uplink and downlink (Wu *et al.*, 2017, Georgiou *et al.*, 2021). Moreover, 5G requires up to 10 times less energy than the previous 4G/LTE mobile communications standard (Andrews *et al.*, 2014, Georgiou *et al.*, 2021). It is expected that the 5G network will have a 1,000-fold rise in traffic in the coming decade, although the energy usage of the whole infrastructure will be just half of today's system's consumption. Therefore, this is a crucial factor for reducing the total cost of ownership, including the environmental impact of the networks (Wu *et al.*, 2017, Georgiou *et al.*, 2021). The Millimeter waves (MMWs) are used to denote radiofrequency (RF) fields above 6 GHz. The increased use of RF fields above 6 GHz, particularly for the fifth-generation (5G) mobile phone network, has given rise to public concern about any possible adverse effects on human health(Karipidis *et al.*, 2021). The evolution of wireless technology

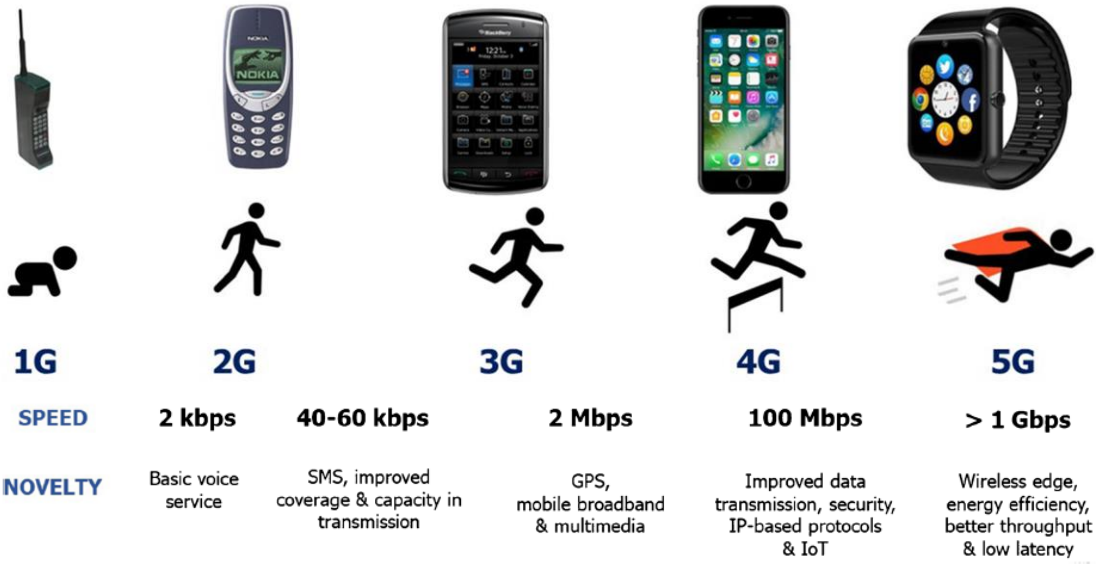

Figure 2: Animation showing the potential areas suitable for implementation of 5G technology to facilitate efficiency and transparency and improve patient safety (Karipidis *et al.*, 2021)

Radiofrequencies interaction with biological systems

Radiofrequencies interaction with biological systems (Valberg *et al.*, 2007) are shown in figure.1.

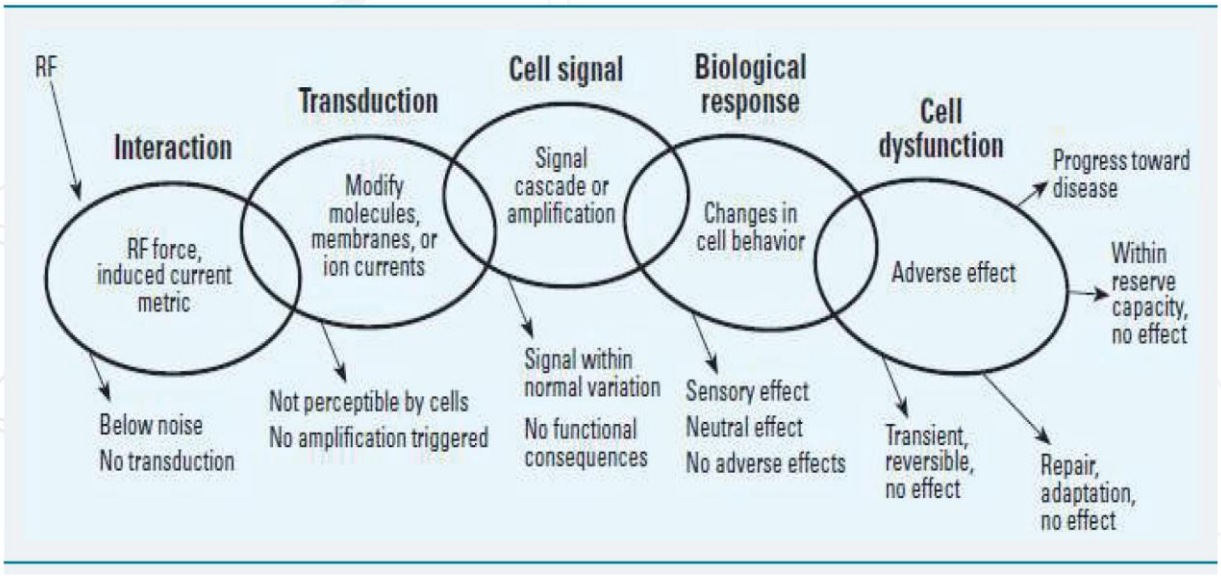

Figure 3: Radiofrequencies interaction with biological systems (Valberg *et al.*, 2007)

Effect of electromagnetic fields on human health

Exposure research studies consider RF power density (W/m2), frequency, duration of exposure, and distance from the source in relation to health effects (Foster, 2007). Russel (2018) reported that non ionizing radiation affects cause non-thermal cellular damage; including DNA integrity, cell membranes, protein synthesis, sperm damage, and immune dysfunction. Also, there is an increasing number of people experiencing electro sensitivity. The author suggests that the thermal effects of 5G could be a concern for the eyes. It concludes that there may be significant consequences to human health. Ebrahim *et al.*, 2016 mentioned that EMFs might produce a variety of adverse in vivo effects such as headaches, chronic fatigue, heart problems, chest pain, nausea, stress, forgetfulness, influence the learning and memory, cardiovascular system, cataracts, reproductive system, CNS, endocrine, immune systems, and sleep disturbances. It have been implicated in adversely affecting multiple facets of human health such as brain cancer, leukemia, lung, and breast tumors, Lou Gehrig's disease, genotoxicity, and neurodegenerative disease, reproduction anomalies, infertility, birth defects, increased risk of miscarriage, childhood morbidity, amyotrophic lateral sclerosis, de novo mutations, depression, Alzheimer's' disease, and suicide. Author concluded that exposure of animals and human to EMFs have been a negative effects on CNS, cardiovascular system, endocrine, immune, and reproductive system, the developing embryo/fetus, and cause a histopathological changes and disturbances in functions of different body organs. Acute exposure to non-ionizing radiation can lead to increased internal temperature, speeds up chemical reactions rate which result in biochemical and physiological effects (Abd El Rahman *et al.*, 2014, Ebrahim *et al.*, 2016, Azab and Ebrahim, 2017a).

Effect of electromagnetic radiation on cell membrane

Electromagnetic radiation (EMR) can alter cell membrane permeability such as changes in calcium, ionic distribution and ion permeability (Walleczek, 1992). Calcium is one of the important signaling substances, and an imbalance of calcium homeostasis can alter many functions of the cell. Previous studies have showed that EMR exposure can alter the calcium channels and receptors on the cell membrane, and influence transport of calcium ions over the cell membrane, which play an important role in cell signaling pathways, and in turn may affect the response of neurotransmitters (Bauréus *et al.*, 2003, Narayanan *et al.*, 2018). It was reported that the number of opened calcium channel increased with the presence of EMFs, which might resulting in the increased intracellular calcium concentration under EMR exposure (Zhang *et al.*, 2007). In addition, the changes of intracellular calcium levels can trigger unusual synaptic action or cause neuronal apoptosis. This in turn can exert an influence on the neurotransmission of learning and memory process (Maskey *et al.*, 2010). As the energy source of the cell, the mitochondrial calcium reaction was influenced by the alterations in calcium signaling pathways in response to the effects of EMR exposure (Bauréus *et al.*, 2003).

Effect of Exposure to electromagnetic fields on skin

Exposure of humans can occur through 5G devices with frequencies above 6 GHz, and may be primarily on the skin and, to a lesser extent, on the eyes. This is due to the very low penetration depth of this MMW. Therefore, it is important to investigate whether there are any health-related effects on the skin and/or effects associated with the skin. These include acute skin damage from tissue heating (burns), but possibly also less acute effects (such as inflammation, tumor development, etc.). Such effects could appear after

prolonged and repeated heating of superficial structures (the skin). This would mean that thermal effects occur that are not due to acute but to chronic damage. It may also be that local exposure causes energy deposition in the dermis of the skin, which may be so great as to affect nerve endings and peripheral blood vessels through warming mechanisms. (Simkó and Mattsson, 2019).

Exposure to electromagnetic fields induces oxidative stress

Electromagnetic radiation of cellular phones may affect biological systems by increasing free radicals and changing the antioxidant defense systems of tissues, eventually leading to oxidative stress (Ahmed *et al.,* 2016, Azab and Ebrahim, 2017a). Exposure to magnetic fields (128 mT, 1 hour/day for 30 days) caused oxidative stress in the DNA of renal tissues. Actually, it was able to disturb the oxidant-antioxidant balance in different rat tissues. This imbalance was observed by a decrease in cytosolic CAT, GPx, and SOD activities and increase in the level of MDA in the liver and kidney of rats (Amara *et al.,* 2007). Electromagnetic waves have been shown to exert their effects on biological systems through generation or increase in reactive oxygen species (ROS), which leads to DNA damage and mutation induction (Okano, 2008, Baharara *et al.,* 2014). Once ROS are produced in mitochondria (Ames, 2004).), they are removed by cellular defenses which include the enzymes superoxide dismutase (Mn-SOD, Cu/Zn-SOD, and extracellular (EC)-SOD), catalase, glutathione peroxidase, peroxiredoxins, and the nonenzymatic antioxidants, like glutathione (GSH), thioredoxin, ascorbate, α-tocopherol, and uric acid (Radi *et al.,*2001). The balance between production and neutralization of ROS levels can increase dramatically, which may cause damage to cell structures leading to behavioral, histopathological and biochemical alterations (Rifat *et al.,* 2014).

Exposure to electromagnetic fields and the risk of cancers

Moon, 2020 reported that among the various health issues related to EMFs, the most important issue is human carcinogenicity. According to the International Agency for Research on Cancer's (IARC's) evaluation of carcinogenic risks to humans, ELFs and RFs were evaluated as possible human carcinogens. However, the World Health Organization's (WHO's) view of EMFs remains undetermined. Moon, 2020 concluded that as well-controlled EMF experiments in children are nearly impossible, scientific knowledge should be interpreted objectively. Precautionary approaches are recommended for children until the potential health effects of EMF are confirmed. The IARC designated RF as Group 2B (possibly carcinogenic to humans) in the 2011 Monograph based on observational human studies from the 1990s examining cell phone use and possible increased risk of certain cancers (gliomas, acoustic neuromas, and temporal lobe tumours) (Interphone Study Group, 2010, IARC, 2013). Previous studies mentioned that exposure to radar, which uses RF fields above 6 GHz similar to 5 G causes effects on reproduction, cancer at different sites, and other diseases (Karipidis *et al.,* 2021). The possible mechanism proposed of how EMFs lead to cancer is the impact of EMFs on free radical combination rates in certain enzymes, such as coenzyme B_{12}-dependent ethanolamine ammonia lyase (Harkins and Grissom, 1994). The enzyme reaction rate may be amplified by a factor of up to 100 (Eichwald and Walleczek, 1996). An alternative mechanism may be the interactions between electric field and airborne pollutant particles. The corona ions emitted from high voltage power lines are able to attach the pollutants and increase their electric charge states, which can be deposited on the skin or in the lung through inhalation (Fews *et al.,* 1999). The basis of the IARC assessment was the large interphone epidemiologic studies as well as case-control studies from Hardell and colleagues, which all used self-reported cellphone use (generally from late 1990s and early 2000s) for the estimate of exposure. These case-control studies (which were each based upon cases with N≈1000-3000) found an increased risk of gliomas, acoustic neuromas, and temporal lobe tumours in users with highest self-reported cell phone use (Interphone Study Group, 2010). After a lifetime of exposure of male rats to 1835 MHz GSM-modulated base station signals at whole-body SARs of 0.001, 0.03 or 0.1 W/kg for 19 hours per day increased incidence of cardiac schwannoma (Falcioni *et al.,* 2018)

Effect of Exposure to electromagnetic fields on the nervous system

Most mobile phones are kept near head during talking mode and are in close proximity to the brain (Odaci *et al.,* 2008, Kesari *et al.,* 2014), and the antenna of a cellular phone emits radio frequency electromagnetic fields that can penetrate 4–6 cm deep into the human brain (Dimbylow and Mann, 1994, Rothman *et al.,* 1996, Kesari *et al.,* 2014). 3G MPs cause a significant biological effects in whole brain function. This is because biological effects mainly depend on various factors, i.e., frequency, power density, exposure system, distance, time, etc (Kesari *et al.,* 2014). 5G is dangerous and will harm every living being. Thousands of studies link low-level wireless radio frequency radiation exposures to a long list of adverse biological effects, including: DNA single and double strand breaks, oxidative damage, disruption of cell metabolism, increased blood brain barrier permeability, melatonin reduction, disruption to brain glucose metabolism, and generation of stress proteins (Burrell, 2020). Baliatsas *et al.* 2012 reported that the symptoms attributed to electromagnetic fields include gastrointestinal issues, pain in the muscles and joints, sweating, neurocognitive disturbances (fatigue, dizziness, tinnitus, headaches, concentration, and sleep

problems), eye burning, nose, ear, and throat issues. RF exposure of sufficient intensity and duration in the frequency range of 3 kHz-10 MHz alters the resting membrane potentials of nervous tissues causing depolarization and subsequent sensory effects (Code, 2015). Low-level RF energy could induce immunological disorders, leukemia, deficiency in the blood-brain barrier, neurological anomalies such as disturbances in sleep, headaches, and difficulty in concentration (Hardell L, and Mild, 2004, Lonn *et al.*, 2004, Salah *et al.*, 2017) and affect the cholinergic system which may be due to a decrease of the intake of choline and activation of endogenous opioid neuroreceptors (Lai *et al.*, 1987, 1989&1991, Salah *et al.*, 2017). Exposure of mice to mobile phones and a digital enhanced cordless telecommunications have caused bioeffects in memory and brain (Fragopoulou *et al.*, 2010, Ntzouni *et al.*, 2011&2013). A side from nerve stimulation known to be related to RF exposure, other neurologic effects have been studied. The RSC reviewed studies that document neurophysiological effects from RF exposure, some of which demonstrate EEG changes in subjects when exposed to RF.23 They noted that experimental exposure doses varied widely, with some meant to simulate "typical" community doses (e.g., below SC6). Sleep EEG changes seem to have the most reproducibility between studies (particularly those conducted by Niels Kuster and Peter Achermann laboratories), though none document consistent clinically relevant health effects of these findings (e.g., decreased sleep, cognitive changes) (MacDonald, 2014).

A few studies documented small changes in blood-brain-barrier permeability with RF exposure, but this was dependent on doses above SC6 where heating occurred, and is therefore of limited relevance in the community settings (Stam, 2010). Hu *et al.*, (2021) mentioned that a certain intensity of microwave radiation can lead to abnormal metabolism of monoamine neurotransmitters in the hippocampus and striatum. As a precursor of norepinephrine, and dopamine is a key neurotransmitter in the hypothalamus and pituitary gland. It is mainly responsible for activity in the brain associated with reward, learning, emotion, motor control, and executive functions. Dopamine also correlates to psychiatric and neurological disorders, including Parkinson disease, multiple sclerosis, and Huntington disease (Sheffler *et al.*, 2021). It has been suggested that dopamine inhibits the secretion of gonadotropin-releasing hormone, and there is an axonal connection and interaction between gonadotropin-releasing hormone and dopamine in nerve endings (Kasture *et al.*, 2018). Deficiency of dopamine in the basal ganglia is seen in patients with Parkinsonism (Gilman and Goodman, 1980). Adult rats undergoing daily EMR exposure for 1 h, with an EMR frequency of 1,800MHz, a specific absorption rate (SAR) value of 0.843 W/kg, power density of 0.02 mW/cm2, induced a significant decrease in dopamine in the hippocampus after 2 months of exposure and 1 month after cessation of exposure. This study indicated that EMR exposure may reduce dopamine production in the hippocampus, affect rat arousal, and contribute to decreased learning and memory ability after exposure to EMR (Aboul Ezz *et al.*, 2013). 32 pregnant Wistar rats were divided into control group, low-dose group (receiving mobile phone radiation for 10-min periods), middle-dose group (receiving mobile phone radiation for 30-min periods), and high-dose group (receiving mobile phone radiation for 60-min periods). Rats underwent periods of radiation three times daily from the day of pregnancy continuously for 20 days. Then, the effects of mobile phone radiation on monoamine neurotransmitters in the brain tissue of fetal mice were studied, with a center frequency of 900 MHz, and a SAR value of 0.9 W/kg. The results showed that the dopamine content in the brain tissue of fetal mice increased in the low-dose group but decreased in the high-dose group, and no significant changes were observed in the middle dose group, which suggested that long-term mobile phone radiation could cause abnormal dopamine content in the central nervous system in fetal mice and might affect the brain development of mice (Ji *et al.*, 2012). Norepinephrine is mainly synthesized and secreted by sympathetic postganglionic neurons and adrenergic nerve endings in the brain.

A small number of norepinephrine is produced in adrenal medulla as a hormone (Silverberg *et al.*, 1978). Norepinephrine can be converted to epinephrine through N-methylation (Zhu *et al.*, 2019). The release of norepinephrine in the brain plays a role in various processes, such as stress, attention, sleep, inflammation, and the responses of the autonomic nervous system (Sheffler *et al.*, 2021). Megha *et al.*, 2015 found that after 30 days (2 h/day, 5 days/week) of continuous 1,800 MHz, 1 mW/cm2 microwave radiation, the levels of norepinephrine and epinephrine in rat hippocampal tissue were significantly decreased, indicating that certain conditions of microwave radiation could lead to a decrease in norepinephrine and epinephrine contents in the brain. Cao *et al.*, (2000) applied 900 MHz microwave radiation to male LACA mice. The radiation intensity used was 0, 1, 2, and 5 mW/cm^2; the SAR values were 0, 0.22, 0.44, and 1.1 W/kg, respectively; mice were exposed for 1 h/day for 35 consecutive days. The results showed that the brain norepinephrine content increased significantly when EMR intensity was 1 mW/cm^2. Authors concluded that low-intensity EMR exposure can cause an increase in norepinephrine content in the brain, which might in theory affect epinephrine content, leading to neurotransmitter production disorders. Long-term exposure to EMR may lead to abnormal norepinephrine and epinephrine contents in the brain, depending on the dose of radiation ((Ji *et al.*, 2012, Hu *et al.*, 2021). Serotonin [5-hydroxytryptamine (5-HT)] is massively synthesized in the gastrointestinal tract (mainly in enterochromafin cells), whereas only a small percentage is produced

within the nervous system. In the brain, 5-HT cell bodies, mainly localized in the raphe nuclei, and send axons to almost every brain region (Charnay and Léger, 2010). 5-HT contributes to the regulation of physiological functions such as mood, feeding, cognition, memory, pain, sleep, and body temperature maintenance (Petkov and Konstantinova, 1986). It was reported that rats were exposed to microwave radiation for 1 h, with a frequency of 2,450 MHz, at power densities of 5 and 10 mW/cm^2. The 5-hydroxyindoleacetic acid (5-HIAA) content in the cerebral cortex was significantly increased after microwave exposure at power densities of 5 and 10 mW/cm2. Consistently, the 5-HT turnover rate was significantly increased in the pons, medulla oblongata and hypothalamus at a power density of 10 mW/cm^2 (Inaba *et al.*, 1992). Li *et al.*, 2015 exposed Wistar rats to 2.856 GHz microwave radiation, with mean power densities of 5, 10, 20, and 30 mW/cm2, separately, three times per week for up to 6 weeks. Spatial learning and memory function, the hippocampal morphological structure, electroencephalogram (EEG) data and neurotransmitter content of rats were tested after the last exposure. The results showed that the content of 5-HT in the hippocampus and cerebrospinal fluid of rats in each radiation group increased significantly from 28 days to 2 months after exposure, and these changes were related to the decrease in learning and memory ability, abnormal hippocampal morphology and abnormal EEG results induced by microwave radiation.

Fujiwara *et al.*, 1978 found that 2.45 GHz high-power microwave radiation caused transiently elevated Acetylcholine (Ach) content in the mouse brain. Lai *et al.*, 1989 found that acute exposure to 2.45 GHz, 0.6 W/kg microwave radiation for 20min caused increased choline uptake activity in the frontal cortex, hippocampus, and hypothalamus of rats. Lai, 2018 reported that neurological effects can be seen as psychological/behavioral changes, e.g., memory, learning, and perception. Morphological, electrical, chemical, and behavioral changes have been reported in animals and cells after exposure to nonionizing electromagnetic fields across a range of frequencies. EMF-induced change in brain electrical activity could lead to different consequences depending on whether a person is watching TV or driving a car. Zhang *et al.*, 2015 reported that exposure to 9417 MHz, 200 V/m, 2 W/kg, 12 hr/day on gestation days 3.5-18, offspring tested at 5 weeks of age increased anxiety-related behavior; spatial memory, and learning deficits in male mice offspring. Aldad *et al.*, 2012 recorded that exposure to 800 and 1900 MHz cell phone radiation, gestation days 1-17 (24 hr/day), tested at 8, 12, and 16 weeks old was caused a hyperactive, impaired memory in mice. Vecsei *et al.*, 2013 found that exposure to UMTS phone-like radiation, 1.75 W/kg, 30 min caused decreased thermal pain perception. Yogesh *et al.*, 2014 mentioned that exposure > 2 hr/day of mobile phone use induced a sleep disturbance, latency, and day dysfunction especially in females. Based on cumulative duration of wireless phone use and RF-EMF dose over one year (GSM and UMTS), use of wireless phone and exposure to RF-EMF caused a change in memory performance (Schoeni *et al.*, 2015).

Effects on the Eyes

Burrell, 2020 mentioned that a 1994 study found that low level millimeter microwave radiation produced lens opacity in rats, which is linked to the production of cataracts. An experiment conducted by the Medical Research Institute of Kanazawa Medical University found that 60GHz "millimeter-wave antennas can cause thermal injuries of varying types of levels. The thermal effects induced by millimeter waves can apparently penetrate below the surface of the eye. A 2003 Chinese study has found damage to the lens epithelial cells of rabbits after 8 hours of exposure to microwave radiation and a 2009 study conducted by the College of Physicians and Surgeons in Pakistan conclude that EMFs emitted by a mobile phone cause derangement of chicken embryo retinal differentiation.

Effect of EMF on hematological parameters

Jbireal *et al.*, (2018) reported that exposure to electromagnetic fields caused a deterioration of RBCs function and metabolic activity, which may be due to an increase of toxicity in specific organs and led to the RBCs' functional failure. The mechanisms by which the EMF cause their bad effects may be by causing imbalance in ionic equilibrium, deterioration in cellular large molecules, and generation of reactive oxygen species (ROS), that can damage cellular components such as proteins, lipids and DNA. Jbireal *et al.*, (2018) presented an overview of the previous works from 1997 to 2018 on the varying effects of electromagnetic fields on hematological data in different species of experimental models and human by using different intensities, frequencies, and different sources of electromagnetic fields for different periods. The hematological parameters are fluctuating across the exposure period to the EMFs suggesting the possible induction of hazardous biological effects during the exposure to the magnetic field. Authors concluded that exposure of human and experimental animals to EMFs causes harmful effects on blood cells. These effects were disturbances in hematological parameters depending on species, the sources of EMFs, intensities, frequencies, and duration of exposure.

The increase in oxidative stress in hematopoietic centers has also been reported due to use of mobile phone (Baharara *et al.*, 2014).

Immune System Effects

A 2002 Russian study examined the effects of 42HGz microwave radiation exposure on the blood of healthy mice. It was concluded that "the whole-body exposure of healthy mice to low-intensity EHF. EMR

has a profound effect on the indices of nonspecific immunity (Burrell, 2020).

Effect of EMFs of cardiovascular system

Exposure to EMF can affect the structure and function of the cardiovascular system and may facilitate myocardial infarction by nuclear changing of cardiomyocytes (Azab and Ebrahim, 2017). It causes a significant increase in the activities of serum lactate dehydrogenase, aspartate aminotransferase, and creatinine phosphokinase enzymes, and blood pressure, heart palpitations, pain, and pressure in the chest area, and an irregular heartbeat decreases in plasma total antioxidant capacity and calcium level (Azab and Ebrahim, 2017). Azab and Ebrahim, 2017 reported that the recent articles regarding the cardiovascular effects of exposure to EMFs might be produce a variety of adverse in vivo effects such as chest pain, heart palpitations and/or an irregular heartbeat, and cardiovascular system disorders. It has been an association between elevated magnetic field exposure and mortality of employer in electric utility industry jobs from arrhythmia-related causes and acute myocardial infarction influence heart rate variability by changing autonomic balance. EMF exposure can affect structure and function of cardiovascular system and may facilitate myocardial infarction by nuclear changing of cardiomyocytes. Also, exposure to EMFs caused a highly significant increases in the activeties of serum lactate dehydrogenase creatinine phosphokinase, and aspartate aminotransferase enzymes, and decreases in plasma calcium level and total anti-oxidant capacity. Azab and Ebrahim, 2017 mentioned that the ECG recording of experimental animals exposed to EMF showed a significantly higher R and T voltages, increase in QRS duration, and prolonged P-R and QT-c intervals. A serious histopathological changes in the heart were seen in experimental animals exposed to EMFs, that include dark brown stain muscle fiber nuclei, increases the number of apoptotic cells, hyperemia muscle fiber degeneration, marked cell vacuolation, distortion of some cardiac myocytes, mononuclear cellular infiltration and histological structure of the myocytes spaces were seen. Ultra structural of the myocardial tissue and sarcomere in experimental animals exposed to EMFs showed that lose of area in sarcomeres, irregular structural of myocardial cells, blebs of mitochondria, and lose of its cristae.

Effects on the Heart

A 1992 Russian study found that frequencies in the range 53-78GHz (that which 5G proposes to use) impacted the heart rate variability (an indicator of stress) in rats. Another Russian study on frogs who's skin was exposed to MMWs found heart rate changes (arrhythmias) (Burrell, 2020). The one exception noted by the RSC was a 2013 study that found marked increases in heart rate when a cordless phone base station was moved close to subjects (Havas and Marrongelle, 2013). Since the RSC review, an additional eight experimental human volunteer studies that examined this issue were identified. Four studies measured an effect, and four did not. Of the four that measured an effect, two small studies (N=46, and N=50) observed small changes to the R-R interval on EKGs during brief exposure to RF below SC6 (Misek *et al.*,2017, Misek *et al.*,2018).

Exposure to EMFs induces harmful effects on testis and reproductive activities

Exposure to EMFs induces harmful effects on testis and reproductive activities (Baharara *et al.,* 2015). Azab *et al.*, 2018 mentioned that male individuals generally carry their cell phones in their pockets close to their testes in standby mode increases the importance of studying the effects of EMF on the male reproductive system. Previous studies showed that exposure to EMFs caused serious patho-physiological changes in the male reproductive system that include decreases in serum levels of testosterone, sperm count, motility, morphometric abnormalities, and significant increases in serum luteinizing hormone level, lipid peroxidation, and DNA damage in sperm cells. Histologically, EMFs caused spermatogonia apoptosis, degeneration in the seminiferous tubules, decreases in the number of Leydig cells, and the height of the germinal epithelium. Also, exposure to EMFs induced a significant increase in catalase, and a significant decrease in histone kinase, glutathione peroxidase, and superoxide dismutase. Authors concluded that exposure of human and experimental animals to EMFs have been a negative effect on the male reproductive system by causing histopathological changes and disturbances in the functions of the male reproductive system. The main cause of infertility in men is oxidative stress. The effect of RF on reproductive outcomes have been studied, with particular focus on testicular function or sperm morphology; the RSC noted that confounding from concomitant heat exposure was often not accounted for and dosimetry poorly quantified. Reviews on female reproductive effects, including adverse pregnancy outcomes, were similarly affected (MacDonald, 2014). Male rats exposed to WiFi transmitters at 2.45 GHz caused a changes in cellular-level sperm parameters in the higher exposure group compared to the low exposure and control groups (9 rats in each group) (Shokri *et al.,* 2015). The second study was of pregnant female mice (N=15) exposed daily to EMF at 50 Hz. The female offspring in the experimental group had oocyte abnormalities compared to the control group (Roshangar *et al.*, 2014).

Developmental Effects

A recent review of 4 large pregnancy cohort studies comprising a study group totalling 55,507 pregnant women and their children, grouped individuals according to self-reported cell phone use (none, low, intermediate, and high) and observed subsequent pregnancy duration, fetal growth, and birth weight. The

study found no increased risk of adverse fetal growth outcomes or birth weight, but did identify a small but statistically significant increased risk (HR = 1.04, 95% CI 1.01, 1.07) for birth at lower gestational age with reported intermediate (but not high) cell phone use (Tsarna *et al.*, 2019).

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