



# Potential Impacts of Radiofrequency Electromagnetic Fields on the Central Nervous System, Brain Neurotransmitter Dynamics and Reproductive System

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**ABSTRACT:** Human life has been increasingly affected by the rapid advancement of electronic technology and the widespread use of devices emitting electromagnetic radiation (EMR), such as Wi-Fi and mobile phones. While much remains unclear, studies suggest that electromagnetic fields (EMFs) can influence human health, particularly reproduction and the nervous system. EMF exposure, including from non-ionizing radiation produced by Wi-Fi and mobile phones, has been linked to potential effects on the male and female reproductive systems, embryonic development, and neuronal health. Key mechanisms include oxidative stress, thermal effects, changes in neurotransmitter metabolism, receptor function, nerve cell apoptosis, and ion channel dynamics. However, the long-term health risks, especially in children and adolescents due to prolonged exposure, remain a topic of debate. Despite current studies not confirming that RF-EMW from Wi-Fi exceeds safety guidelines, further research is essential to fully understand the implications of RF-EMW exposure on human health, particularly regarding reproduction and neurological effects. This review highlights the need for updated safety standards, more refined regulatory frameworks, and long-term investigations to clarify the potential biological and neurobiological consequences of EMF exposure.

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## 1- Introduction

Electromagnetic radiation and electromagnetic fields are an integral part of both natural and man-made environments and, as such, in tight connection with the lives of individuals. The Earth is naturally wrapped by a geomagnetic field generated via the action of solar winds with the magnetic core of the planet—a fact influencing every living organism here on Earth. Within the last years, artificial electromagnetic waves have been produced with the development of technology—manifestation that has its roots in an experimental identification by the scientist Heinrich Hertz. Further, this accelerated the electromagnetic technologies applied so broadly in communication, medicine, and industry. With rapid development and use of modern electronic devices, such as smartphones, and wireless methods of communication, human exposure to artificial EMFs is greatly increased and becomes a global issue concerning their potential health effects and modern environmental stressors. Electromagnetic waves vary in a spectrum from ionizing to non-ionizing radiations. [1-4]

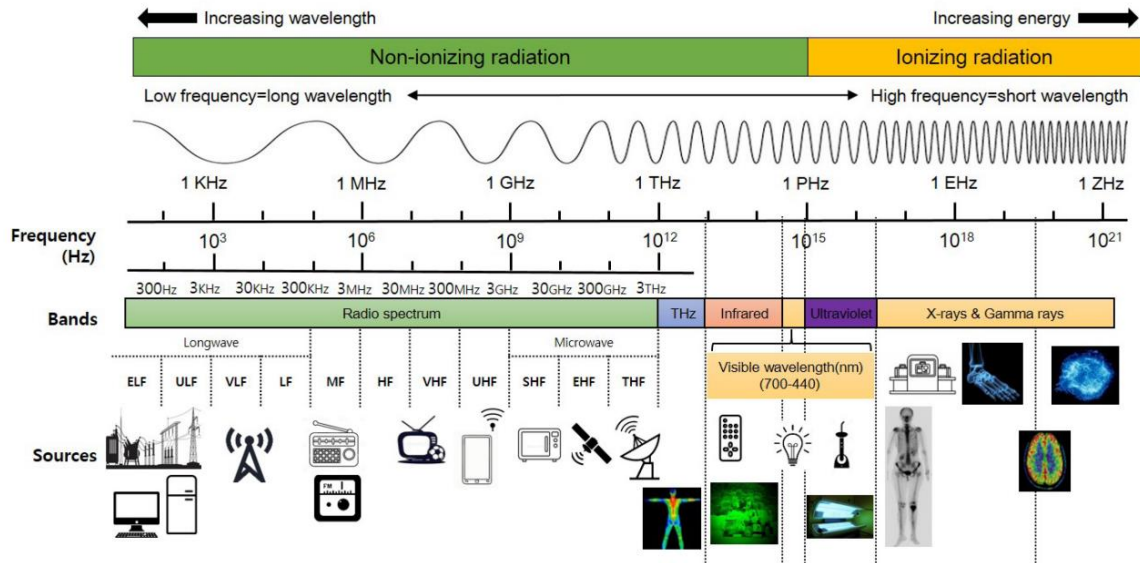
The ionizing high-energy waves like X-rays and gamma rays are well documented to produce ionization with health associated risks. Nonionizing radiation, however includes ultraviolet light, visible light, microwaves and radiofrequency waves applied in everyday application mainly

in communication and household devices. Those with RF-EMFs have frequencies from 30 kHz up to 300 GHz, and of those highly relevant because of the pervasiveness of their presence are those with extremely low frequency, from 3 Hz up to 3 kHz. Interest in biological system influences, above all nervous system, of RF-EMFs has set off serious scientific debates. This value is considered one of the most important physical measures related to the quantification of EMF exposure, as it describes the energy absorbed by biological tissues in a radiofrequency energy exposure period. SAR values strongly depend on factors such as frequency, kind of tissue, and polarization; the wide variation of measured values underlines how complex the study of the interactions between EMF and biological systems could be. The most sensitive of organ systems to electromagnetic exposure includes the nervous system, with the brain being one of the prime focuses of study. Neurotransmitters—those neurochemicals that transmit impulses across neurons—enable cognition, emotion, and other works of the brain. [5-7]

There is evidence that EMFs alter neurotransmitter metabolism, transport, and receptor function, important to neural circuitries. An imbalance of neurotransmitter homeostasis—mainly those critical neurotransmitters of dopamine, serotonin, glutamate, and GABA—would most likely be in relation to neurological disorders, such as depression and schizophrenia, even neurodegenerative

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**Fig. 1. Diagram showing the range of electromagnetic fields present in our surroundings. [10].**

diseases like Alzheimer’s and Parkinson’s diseases. RF-EMFs had been indicated to disturb neurotransmitter homeostasis throughout various areas in the brain that could influence both neurodevelopment and cognitive functions. Although these results are obtained, the mechanisms behind these effects are poorly understood, and inconsistencies in studies make it even more confusing. These EMF exposures have increased in everyday human life and induce public panic from contradictory research outcomes. In May 2011, RF-EMFs were classified as possibly carcinogenic to humans, Group 2B, by the IARC, which has raised more debates concerning health issues. Whereas a number of studies have explored the possible associations between EMFs and cancer, genetic damage, immune dysfunction, and neurological disorders, the clear evidence has remained elusive. [8]

This uncertainty has provided fuel for disquiet not only in the scientific community but also among the general population. The widespread use of these RF-emitting devices, especially among younger people, has increased even more the need to clarify their long-term effects. Recent research has pointed out that RF-EMFs can directly act on neuronal activity both directly on the nerve cells themselves and indirectly via thermal mechanisms; thus, their possible effects on neurodevelopment and brain functions should be studied. Since exposure to EMF has become unavoidable in daily life, the understanding of its biological effects has assumed increasing urgency. How EMFs modulate neurotransmitter systems and neural activity is an important investigation that needs to be carried out for the elucidation of their implications for human health. Such gaps in knowledge regarding the unraveling of the interaction mechanisms between EMFs and the nervous system require comprehensive and methodologically sound research. This review synthesizes the current findings related to the influence of EMFs on brain

neurotransmitters, which may throw light on possible health implications and the importance of further research in this fast-evolving field. [9]

It is with this in mind that we hope to present a comparison of recent researches specially [10], [11] and [12] papers, consolidate their data, research findings, and results, and analyze them for better understanding of how the central nervous system and neurotransmitters of the brain are affected by these waves. A Comparative and Review Article on Recent Research. The next section will be another section, “The Effects of These Waves on the Human Reproductive System,” that will focus on male and female reproductive systems. This section will require a parameter defined as SAR. The SAR expresses the quantity of electromagnetic radiation absorbed per unit mass per time and provides a basis for establishing safe exposure limits. SAR values are expressed for parts of the body and an average value is calculated for the whole body.

$$SAR = E^2 \frac{\sigma}{\rho} \left[ \frac{W}{kg} \right] \quad (1)$$

where:  $\sigma$  is electric conductivity of the sample (tissue) in S/m,

$E$  is value of electric field strength in V/m,  $\rho$  is density of the sample in  $kg/m^3$ .

The last section will be a general conclusion and will introduce some ideas for the future.

## 2- Preliminaries

With rapid industrial development, the use of communication devices, especially wireless devices like

smartphones, is growing fast. This has caused increased public concern over possible biological hazards related to the electromagnetic fields of these devices. The human health effect of the electromagnetic field emission has risen as a concern because smartphones are kept close to the body and their use has increased manifold among most age groups, including children. The IARC has classified RF-EMFs as possibly carcinogenic, and several studies have indicated long-term exposure to RF-EMFs can cause neurological effects like headaches, sleep disturbances, cognitive disorders such as memory loss, and changes in EEG patterns. Besides this, a number of biological alterations have been reported in a number of radiofrequency-EMF studies using animal and cellular models, such as increased autophagic activity in neurons, changes in ion-channel expression, and even impairments to myelin sheath. More specifically, increased levels of proteins related to autophagy are recorded in the hippocampus—an area very crucial in learning and memory—after exposure to RF-EMF, thereby indicating that there is some adaptation in the brain against electromagnetic stress. While these studies no doubt carry a lot of information, most are either animal or cell models, whose relevance to humans is very much uncertain. More epidemiological studies should be done to establish what actually happens when RF-EMF is applied to the human body, and limits of exposure should be more clearly issued. [13-18].

### Electromagnetic Radiation

The presence of a variety of sources of electromagnetic radiation, including Wi-Fi devices, in the environment has created the need to develop legal frameworks for the protection of environmental health. In Poland, the main legal act regulating radiation safety issues is the Environmental Protection Law of 27 April 2001 (Journal of Law 2019, item 1396, as amended) [19]. According to Article 122 of this act, admissible levels of electromagnetic field in residential and public areas are determined by the Regulation of the Minister of Health of 17 December 2019 (Journal of Law 2019, item 2448) [20]. On a wider scale, the European Union has adopted the Council Recommendation (1999/519/EC) of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0 Hz to 300 GHz). In Polish regulations and in the EU recommendation, identical reference levels of electromagnetic field (electric field strength, magnetic field strength, and equivalent plane wave power density) are established in this frequency range. In the frequency range between 2 and 300 GHz (thus covering the radio frequencies employed by Wi-Fi), the electric field strength should not exceed 61 V/m, while the plane wave power density is limited to 10 W/m<sup>2</sup>. With this, Poland's norms on radiofrequency electromagnetic field exposure became among the most severe in the world by the end of 2019. These are legal documents that outline both the basic restrictions directly affecting human health and the reference levels for monitoring and assessing any exceedance of these restrictions. In the European Union's recommendation, the basic restrictions are quantified by the specific absorption

rate or SAR, a measure of the rate at which the human body absorbs radiofrequency electromagnetic fields, in W/kg. The EU and the International Commission on Non-Ionizing Radiation Protection recommend the following as the permissible average SAR for the whole body: 0.08 W/kg for frequencies between 10 MHz and 10 GHz. The localised SAR is permitted to be 2 W/kg for the head and torso, and 4 W/kg for the limbs [21]. The usual purpose of SAR is the assessment of exposure from devices emitting electromagnetic radiation in proximity to the body. However, the calculation of SAR is a complex issue due to its dependence on body thermoregulation properties, where tissues are capable of dissipating the absorbed thermal energy. These reference levels, which are given in terms of electric field strength, E; magnetic field strength, H; and equivalent plane wave power density, S, guarantee that, for exposure below these values, the basic restrictions are not exceeded, independent of exposure duration.

### WIFI

Wi-Fi is a wireless communication technology designed for local area networking, operating within the 2.4- and 5-GHz radio bands, which are in the microwave frequency range similar to those used in mobile telecommunications. Over recent years, Wi-Fi has become an integral part of modern life. Wi-Fi-enabled devices support wireless local area networks (WLANs), with the most common application being the provision of internet access to portable devices such as laptops. However, Wi-Fi is also used in a wide range of other communication devices, including smart electricity meters. Initially developed as a wireless alternative to Ethernet cables, which were previously used to connect computers to local networks, Wi-Fi has now become the foundation of nearly all WLANs in homes, offices, and other environments. Today, virtually every modern laptop and smartphone is equipped with Wi-Fi capabilities. Additionally, many household appliances—such as bathroom scales, gaming consoles, and audio systems—are now Wi-Fi-enabled to facilitate remote programming and control [22]. Wi-Fi's widespread use is further driven by its convenience, as it allows users to move freely while using various mobile devices. Figure 1 illustrates a basic WLAN diagram. A Wi-Fi router may be implemented in combination with an access point or as a separate device that allows connecting to a wireless network. Most Wi-Fi devices use the frequency range of 2.400–2.4835 GHz (2.4 GHz). This range is close to the frequency band used by mobile phones, for example, the 2.1 GHz band for 3G networks. Wi-Fi signals operate within the ISM (Industrial, Scientific, and Medical) band. This 2.4–2.5 GHz frequency range is also allocated for usage by other devices, which include communications devices like cordless phones, and household appliances such as microwave ovens. Sometimes, however, Wi-Fi may employ the higher range of 4.915–5.825 GHz - otherwise known as 5 GHz [23]. To estimate the exposure to radiation emitted by a Wi-Fi device, a simple model representing the propagation of electromagnetic radiation in free space can be used. For

**Table 1. Attenuation values of building materials for the 2.4 GHz frequency [24].**

Element	Material	Thickness [cm]	Attenuation [dB]
Ceiling	Concrete	30	11
External wall	Brick	30	9
Internal wall	Brick	10	7
Partition wall	Plasterboards	7	2
Door	Wood	4	2.5

an antenna emitting power (P), excluding reflections from surrounding surfaces, the power density (S) at a distance (R) can be calculated using the following formula:

$$S = \frac{PG}{4\pi r^2} = \frac{EIRP}{4\pi r^2} \quad (2)$$

where:

- G is the gain of the antenna (expressed in dBi) which indicates the value (expressed in dB) at which the antenna gain is greater in relation to the hypothetical isotropic antenna (an infinitely small point in a vacuum, emitting isotropic electromagnetic radiation in each direction without reflections or losses);
- EIRP is the effective isotropic radiated power, which is the product of power (P) and gain of the antenna (G) and represents the power that the isotropic antenna would have to radiate in order to get the same level of the signal in the direction of the maximum radiation of the given antenna;
- R is the distance from the source of electromagnetic radiation.

Assuming that the antenna is a basic, lossless dipole antenna—a fairly typical variety for most Wi-Fi devices—the gain of the antenna, G, is equal to 1.65. This means that typical devices, running at 0.1 W of power, create maximum power densities of 330 mW/m<sup>2</sup> and 13 mW/m<sup>2</sup> at 20 cm and 1 m away, respectively. This power density was calculated by an equation that doesn't take the reflections from surrounding surfaces into account, which is one major factor affecting the propagation of radiofrequency electromagnetic waves indoors; it will provide, however, reasonable estimates for wave propagation at distances of a few meters from the antenna within the building. Keep in mind that Wi-Fi transmitters in realistic situations, do work at power level far lesser compared to the estimated values obtained above equation.

In real conditions, electromagnetic waves propagate indoors far from free-space conditions. These waves interact with obstacles such as walls, furniture, and even people.

Also, some physical phenomena can be identified, such as wave attenuation, reflection, and diffraction by the edges of the walls. Table 1: Attenuation values of various building materials in the 2.4 GHz frequency. For example, a 3-dB attenuation represents a doubling of signal loss, a 9-dB attenuation causes an eightfold reduction, and an 11-dB attenuation represents a 12-fold loss of signal in the selected frequency range. The antennas involved in such devices, like laptops or other Wi-Fi-enabled devices, are small, only a few centimeters in size, and thus negligible compared with the distance between these devices and the human body. This would mean that the exposure to electromagnetic radiation from these devices decreases rapidly with increasing distance between the user and the device (exposure decreases inversely with the square of distance). However, it should be mentioned that the users of Wi-Fi devices are usually farther from these devices compared to the users of mobile phones, in which the device is kept near the head [25].

### 3- Recent Researches and Studies

Recent research into the possible adverse effects of electromagnetic radiation, especially at radio and microwave frequencies, has normally considered measured exposure quantities such as electric field strength and equivalent plane wave power density, which are directly compared with the reference levels in the relevant legal limits. In alternative approaches, the specific absorption rate (SAR) is calculated as the direct quantity for the influence of radiation on human tissue [26]. The effects of electromagnetic radiation generated by Wi-Fi devices have been studied mainly for two purposes: to assess the exposure under normal usage conditions or to evaluate it under extreme conditions, like continuous antenna emission and positioning a few centimeters away from the body. Experimental measurements and numerical simulations have been performed, some of which included animal testing. Summaries of the key findings are underlined below.

A 2017 study measured the exposure to electromagnetic radiation from Wi-Fi and other sources in 23 schools across Australia. The authors calculated both mean and peak values of radiofrequency electromagnetic radiation. All measurements were found to be significantly lower than the reference

levels outlined in the Council Recommendation (1999/519/EC), which limits public exposure to electromagnetic fields (0 Hz to 300 GHz). The measured exposure levels in empty classrooms and those with students ranged from about 0.0001% (average) to 0.01% (peak) of the recommended limit values. These were very low levels compared to those related to other common devices, such as radios, televisions, or mobile phones [27].

In the study conducted in 2011, electromagnetic radiation of electric field strength from 15 active laptops and 12 Wi-Fi access points at UK schools was measured. At 0.5 m away from the devices, maximum electric field strengths were estimated at 2.893 mV/m for laptops and 5.716 mV/m for Wi-Fi routers, representing only 0.005% and 0.01% of reference levels recommended by the European Union. It showed that the equivalent plane wave power density at the same distance was 22 mW/m<sup>2</sup> for laptops and 87 mW/m<sup>2</sup> for Wi-Fi routers. Such values are well below recommended exposure limits and constitute 0.22% and 0.87% of the reference levels specified in Polish and European regulations, respectively. Further measurements were conducted over larger distances (beyond 0.5 m) and demonstrated that by doubling the distance to 1 m, power density decreased by about fourfold. Such a result is expected as it follows the rule that radiation exposure decreases with increased distance from the source.

Foster [28] conducted a comprehensive study of the electromagnetic radiation emitted by Wi-Fi devices across various environments and countries. In all, 365 measurements were taken in 55 cities across four countries: the United States, France, Germany, and Sweden, in various settings, including offices, shops, and healthcare facilities. These levels have proved to be much lower than those allowed, according to

international legal limits, at close distances, like 1 m from laptops, where the signal is maximal. In this context, the measurements had been recorded for scenarios including large download of files (to hold the devices in maximal power conditions). The equivalent plane wave power density of the radiation was rather low compared to exposure limits according to both Polish and international recommendations, by an order from 0.001 W/m<sup>2</sup> up to only 0.01 W/m<sup>2</sup>, thus giving only 0.01% to 0.1% of the recommended limit values.

Another study [29], in 2007, measured the exposure to electromagnetic radiation in indoor environments such as cafes, airports, and open spaces - including public areas with internet access, such as downtown areas and residential zones - in Germany. In all cases, the equivalent plane wave power density was several orders of magnitude lower than the established limits. Even at a distance of 20 cm from the devices-as in, for example, cafes-the values measured were well below the recommended limits. In open spaces with considerable distances from the devices, exposure levels were far lower than those recorded in indoor rooms. The specific results are provided in Table 2.

In 2010, an experiment was conducted with the use of a voxel hantom, a computer-simulated model of a 10-year-old child's body, simulating exposure to electromagnetic radiation from Wi-Fi devices operating at 2.4 GHz and 5 GHz. The results of this study showed that the SAR values were considerably lower than in the limits laid down by relevant regulations. The highest measured SAR value for the whole body was 19.1  $\mu$ W/kg, normalized for 1 V/m electric field strength. From this, it was concluded that to exceed the limit for the whole body, 0.08 W/kg, the electric field strength should be 64.7 V/m. Typical values of electric field strength

**Table 2. Maximum measured values of equivalent plane wave power density at various measuring points [29].**

Measurement location	Minimum distance from the antenna [m]	Maximum measured values of equivalent plane wave power density [ $\frac{mW}{m^2}$ ]	The share of the measured value in relation to the limit value $10,000 \frac{mW}{m^2}$
Cafe	0.2	183	1.83%
Airport	3.0	1.86	0.0186%
Outdoor 1 downtown	5.0	0.10	0.001%
Outdoor 2 downtown	5.0	0.34	0.0034%
Outdoor 1 residential area	50.0	0.002	0.00002%
Outdoor 2 residential area	50.0	0.004	0.00004%

measured at a distance of 1 m from Wi-Fi access points were well below 2 V/m, far lower than the threshold required to exceed the SAR limit. SAR values were also measured at various distances from the antenna, including for the head and torso. Even at the shortest distances, such as 3 cm between the head and the antenna, the maximum SAR measured was 81.7 mW/kg. Assuming typical Wi-Fi antenna power of 10 mW for laptops, the SAR values were well below the 2 W/kg limit set by the International Commission on Non-Ionizing Radiation Protection for the head and torso. These values measured in this study were just about 4% of the recommended limit [30].

In addition to studies under normal operating conditions, a number of experiments have been conducted at higher levels of exposure, for example, when the devices are close to the body or operating at maximum power. A study by Kuhn et al. 2007 evaluated electric field strength and SAR levels for Wi-Fi devices under worst-case conditions, with the devices operating at maximum power. In the case of Wi-Fi routers operating in the 2.400–2.484 GHz frequency band, electric field strength was measured as 1.1 V/m and for the 5.200–5.800 GHz band, it was recorded at 0.9 V/m. SAR values of 0.36 W/kg and 0.81 W/kg, respectively, were obtained, lower than the reference levels and basic restrictions. The study suggested that keeping such devices at a greater distance, such as mounting them on a wall above users' heads, could further reduce exposure.

A study by Schmid analyzing various devices including baby video surveillance systems, DECT (Digital Enhanced Cordless Telecommunications) phones, Bluetooth devices, and Wi-Fi routers has conducted. The results showed that the equivalent plane wave power density measurements at all monitored points were well below the regulatory limits, with average values constituting only 0.004% of the limit values. The study also measured SAR values under adverse conditions where a device (such as a Wi-Fi laptop) was in direct contact with the phantom's surface. The maximum SAR value recorded for the laptop was 0.05 W/kg, which is well below the SAR limits for the head and torso (2 W/kg) and for limbs (4 W/kg) [30].

In addition to studies measuring physical quantities related to exposure to high-frequency electromagnetic radiation, experiments involving living organisms—such as animals and humans—have also been conducted to assess the biological effects of Wi-Fi radiation. A study by Banaceur et al. in 2013 exposed mice to Wi-Fi radiation at 2.4 GHz, aiming to reach an SAR of 1.6 W/kg for 2 hours a day over a period of one month. The results indicated that the exposure improved memory in animals with Alzheimer's disease and enhanced cognitive abilities. In a similar vein, Shokri et al. (2015) conducted experiments on rats by dividing them into three groups: the first group was not exposed to electromagnetic radiation, the second was exposed for 1 hour a day at 2.45 GHz for 2 months, and the third for 7 hours a day over the same period. The study showed the impact of the duration of exposure; sperm quality was damaged due to this factor. Its deterioration was most apparent in the third group of the experiment. The conclusion here is that

the effects of electromagnetic radiation exposure depend on time. However, because the statistical sampling was small, no weight was given to such results of this work [31], [32].

Studies conducted in 2017 assessed the impact of long-term exposure to electromagnetic radiation emitted by Wi-Fi devices on the ability of rats to learn. Results from this work indicated that the Wi-Fi signals negatively affected the recognition of a novel versus familiar object by the animals. The interpretation of this finding was an indication of the negative potential of electromagnetic radiation from Wi-Fi; thus, an investigation was proposed into the effects of electromagnetic radiation on cognitive behaviors in both animals and humans [32].

Most studies dealing with this issue in animals have indeed reported harmful effects of electromagnetic radiation, although results from these studies have usually been inconsistent. It is already known that electromagnetic radiation results in the absorption of energy by living tissues and may induce changes in hormone levels or even the activity of nerve endings in the brain of exposed organisms, even without thermal effects of the radiation. When SAR values are relatively high, about 6.8 W/kg, a definite decrease in life span of the exposed animals is predicted.

Table 3 shows some biological effects of high-frequency electromagnetic radiation on various organisms for different values of SAR. When low levels of electromagnetic radiation are absorbed by animals, as long as the resulting body temperature does not rise, the thermoregulatory mechanisms of the animal may be able to dissipate the excess heat. In primates, exposure can cause behavioral changes, like reduced locomotor activity or delayed reaction times. However, the threshold values for these behavioral changes are merely indicative. Previous research has generally suggested that high-frequency electromagnetic radiation is a weak biological factor [33]. Ethical constraints make it difficult to conduct studies on the effects of radiofrequency electromagnetic radiation on human health.

In addition, the optimal test conditions—full device power range, long-term studies on the same population—are difficult to establish [35]. For these reasons, experiments are limited to animal models or cell cultures, each of which presents its own set of restrictions. It is also unknown if, and to what extent, the conclusions drawn from animal experiments carry over to humans, adding to the ambiguity of many of these studies.

A more recent 2019 study involving humans investigated the possible effects of short-term Wi-Fi exposure on cognitive functions. The study was approved by the local Ethics Committee of Shiraz University of Medical Sciences, Iran, and was registered with the Iranian Registry of Clinical Trials. Forty-five students at Shiraz University were exposed to Wi-Fi in a sham-controlled environment ( $n = 45$ ), in two two-hour sessions. After Wi-Fi exposure, participants were checked for reaction time, short-term memory and reasoning capability. No significant impact of Wi-Fi signals is found when comparing the average response against the sham conditions. In the experiment, reference levels of electric

**Table 3. Examples of biological effects caused by high-frequency electromagnetic radiation [34].**

Type of biological effect	Research subject	SAR [W/kg]	Temperature increase [° C]
Cataract	Rabbits	100-150	3-6
Congenital abnormalities	Rats	6-10	2-3
Hormonal responses	Rats, primates	3-4	1-2
Impaired performance of learned activities	Rats, primates	2-5	1
Reduction of locomotor activity	Primates	1-3	<1
Activation of thermoregulatory mechanisms	Primates	0.7-1	<1
Decreased metabolism	Primates	0.7-1	<1
Auditory hallucinations	Humans, rats	0.01-0.1	-
Electrocardiography changes	Rabbits	0.01-0.5	-
Increased permeability of the blood-brain barrier	Rats, rabbits	0.05-0.1	-

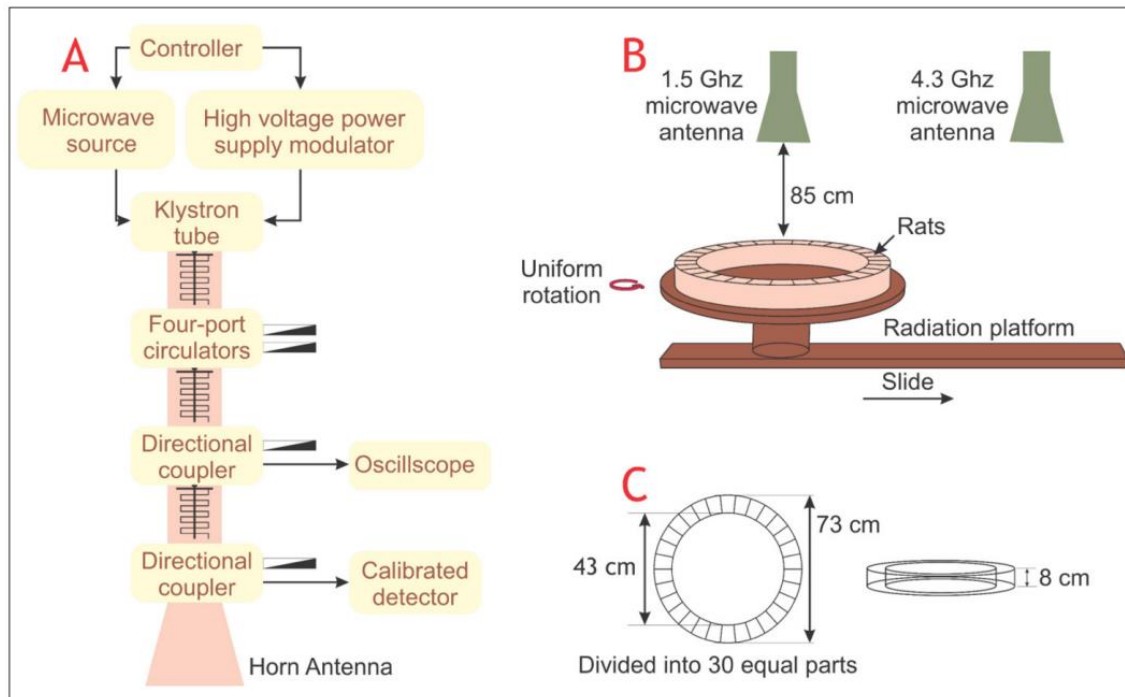
field strength and equivalent plane wave density were also measured. At a distance of 1.5 meters and a height of 1.2 meters (typical of Wi-Fi device usage), the values were 4.1 V/m and 0.0446 W/m<sup>2</sup>, respectively. These values constituted only 7% of the limit for electric field strength and 0.4% of the limit for equivalent plane wave density as laid down by many European Union countries [36]. Since the 1950s, there have been many studies conducted to assess the biological effects of radiofrequency electromagnetic radiation, including from mobile phones and Wi-Fi devices [37]. None have definitively proven any risk associated with the use of these devices, provided that the relevant legal limits (including basic restrictions and reference levels) are not exceeded. Electromagnetic waves can be categorized, according to wavelength, into ELF-EMF, RF-EMF, and Microwave Radiation. ELF-EMF, with frequencies between 3 and 3,000 Hz, is generated from household electronics, electric wires, and high-voltage power lines. RF-EMF, with frequencies between 100 kHz and 300 GHz, is given off by devices such as mobile phones, Wi-Fi, and radio systems. These devices are increasingly applied in everyday life, which only increases exposure to RF-EMFs. When exposed to the human body, these waves might be absorbed on interaction; the quantity of energy absorbed, expressed per unit mass of tissue, is known as Specific Absorption Rate (SAR). RF-EMFs can penetrate and induce oscillations within charged molecules, a process with possible health threats, especially at mobile phone frequency. There are national and international standards regulating such exposure levels, and South Korea enforces a safety standard of 1.6 W/kg, said to be 50 times stricter than the hazard level expected. [38-44]

### Effects OF EMF on Cancer

The studies also considered the links of EMF exposure to cancer and its various manifestations. In the main, epidemiological studies have not been able to demonstrate any appreciable increased risk of leukemia in children and brain tumors in adults from exposure to ELF-EMF and RF-EMF. However, there is still concern over the possible carcinogenic effects of RF-EMF, especially in relation to the cranial nervous system, since mobile phones are placed near the head. Some have suggested that long-term mobile phone use may elevate the risk of brain tumors, such as gliomas and acoustic neuromas, while others have shown no such association. The lack of evidence for the carcinogenicity of RF-EMFs partly reflects the relatively short period for which many people have used mobile phones and the long latent period needed in epidemiological studies for the effects of prolonged exposure to be discerned.

### Genotoxic Effects of EMF

Apart from carcinogenesis, RF-EMF exposure is also linked to genotoxicity through the induction of DNA oxidative damage, fragmentation, and strand breaks. All these genetic changes were noted in various cellular components such as neurons and lymphocytes, possibly leading to genetic disorders and carcinogenesis. Chromosomal instability and gene mutations are also reported upon RF-EMF exposure. Studies regarding the effect of RF-EMFs on the blood-brain barrier reported increased permeability, which may facilitate the passage of substances into the brain. On the other hand, there is controversy in these findings because some studies have found changes in BBB permeability while others did not



**Fig. 2. The experimental setup for RF-EMR exposure includes a microwave source (A), radiation process (B), and a rat container (C). [12].**

report any significant effect. The influence of RF-EMF on the BBB is being studied presently, and more research is needed to clarify its potential risks.

### Effects of EMF on the Blood-Brain Barrier

RF-EMF also has effects on brain functions like stress, anxiety, and memory. Animal models have demonstrated that RF-EMF acts to alter benzodiazepine receptors related to stress and anxiety. Where some studies propose a possible contribution of RF-EMF-induced changes at the BBB to these effects, other studies suggest the dependency of observed effects depending on SAR levels and signal intensity. The inter-relationship among RF-EMF exposure, permeability of the BBB, and cognitive performances remains complex and is still open. To fully realize the biological effect of RF-EMF, it is significant that more comprehensive studies be conducted, taking into consideration factors such as SAR, duration of exposure, and interaction of genetic and environmental factors.

**Conclusion** While health concerns, especially carcinogenicity, genotoxicity, and effects of RF-EMF exposure on the brain, are growing day by day, findings from the research done so far present conflicting evidence: while some point to adverse effects, in other cases, no clear evidence is found. Such interaction with RF-EMF and biological systems, such as a BBB and neuronal activity, discussed here, further needs detailed research. The widespread use of mobile phones and other electronic devices calls for addressing knowledge gaps and developing regulations concerning safe exposure limits.

### Effects of EMF on Learning and Memory

RF-EMF exposure, mostly due to mobile phones, has been reported to be associated with a variety of neurological effects including headache, sleep disturbance, alteration in the brain wave and blood pressure. The reason these effects occur might be that the cranial nervous system is very close to where the phone rests during usage. However, although this was cited to cause cognitive disturbances like memory loss, inability to concentrate, and dizziness in both humans and animals, findings were still inconsistent. Studies on rodents, especially those using behavioral procedures like learning and memory tasks, provide evidence that RF-EMF exposure at particular frequencies could suppress cognitive performances such as spatial learning and memory. Other studies did not show any evident memory change after the same or similar exposure. Several reports of alteration in the hippocampal electrical activity responsible for the learning process following the exposure of low-intensity RF-EMFs; however, the overall cognition result is not predictable. Zhu et al. exposed adult male Wistar rats to 1.5 GHz and 4.3 GHz RF-EMR shown in figure 1, found that it may result in cognitive impairment with damage in the hippocampal tissue. The combined frequencies of both caused more damage, but the frequency itself didn't affect the severity.

### Thermal Effects of EMF Exposure to Brain

RF-EMF is thought to be exposed with thermal effects to the brain that might affect neuronal activity due to the heat generation. This could lead to enhanced glucose metabolism, altered cerebral activity, as was related with brain imaging

following RF-EMF exposure. Thermal effects of mobile phones are also thought to interfere with neuronal activity by heating, which can damage sensitive organs such as the eye. However, further research is required fully to understand the implications of such exposures on health.

**Effects of EMF on Neuronal Calcium Channels**

RF-EMFs also have the ability to alter the functionality of neuronal calcium channels, which are involved in the regulation of neuronal activity and neurotransmitter release. Such disturbances in the functions might further disturb cognitive functions and neuron communications. Indeed, some studies have already demonstrated that RF-EMF exposure increased or decreased calcium channel activities depending on the form of exposure, hence potentially changing neurophysiological processes. Such changes may, in theory, affect memory and behavior, particularly in developing animals, although clear evidence in humans is still lacking.

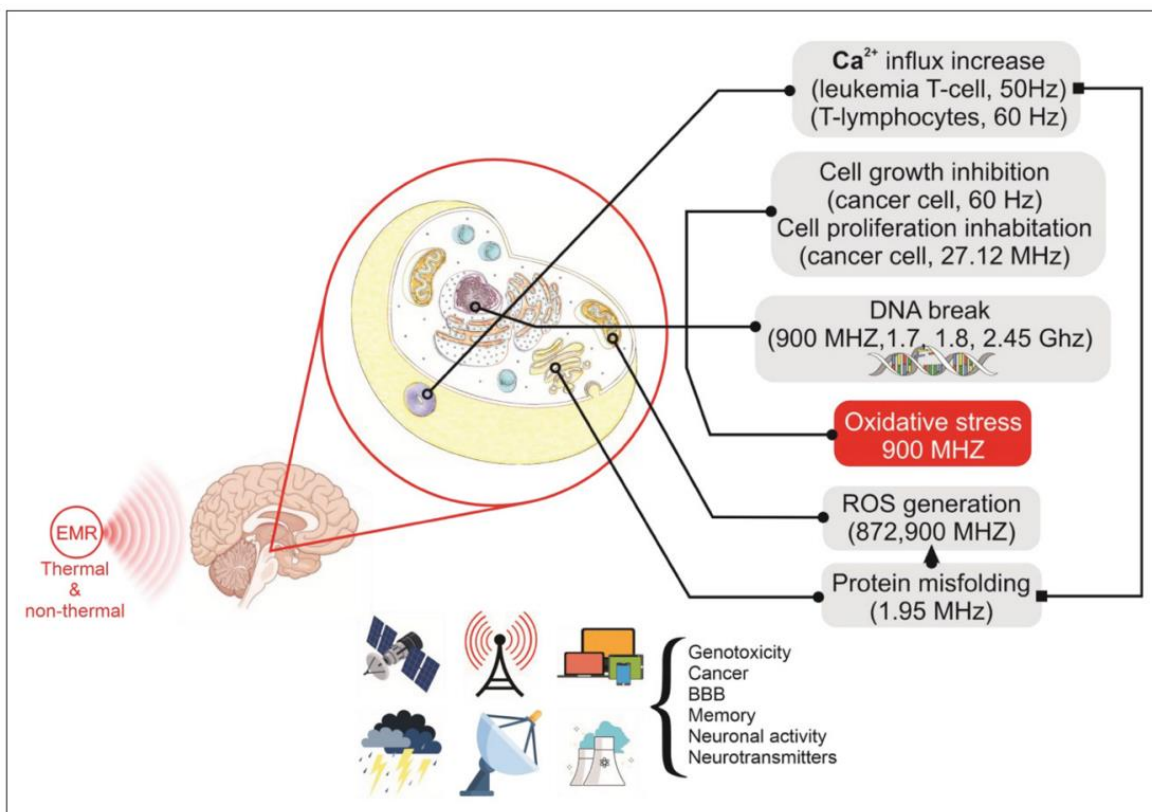
**Effects of EMF on Myelin Sheath**

Finally, RF-EMFs can also affect the myelin sheath, which is critical to the functioning of the nervous system. Some papers conclude that RF-EMF exposure causes structural changes in the myelin protein and impaired myelinogenesis, presenting symptoms of electro hypersensitivity and possible long-term damage to the nervous system. Surprisingly, there

are also studies that show electromagnetic stimulation might promote remyelination and prevent nerve damage in some neurological disorders. Overall, RF-EMF-induced neuronal health disturbances, such as disturbances in learning, memory, and myelin sheath, remain active areas of research, which must be complemented by additional research to establish not only the risk but also the therapeutic benefits of RF-EMF exposure.

**Effects of EMF on Autophagic Activities in Neuron**

Electromagnetic radiation (EMR) exposure has been increasingly recognized for its potential impacts on various biological systems, particularly the central nervous system, where it can disrupt the normal functioning of neurotransmitters. These neurotransmitters—dopamine (DA), norepinephrine, epinephrine, and serotonin (5-HT)—are crucial for regulating key brain functions such as mood, cognition, motor control, and emotional responses. Dopamine, for instance, plays a vital role in reward processing, motor control, and executive functions, and is implicated in several neurological and psychiatric disorders, including Parkinson’s disease, schizophrenia, and Huntington’s disease. Research has shown that exposure to EMR can lead to significant alterations in dopamine levels, particularly in regions of the brain like the hippocampus and striatum, which are critical for learning, memory, and motor functions.



**Fig. 3. Provides an overview of the effects of RFEMR exposure on the central nervous system (CNS). [12].**

### **Effect of EMR on Dopamine (DA)**

Studies on rats exposed to microwave radiation, particularly at frequencies of 900 MHz and 1,800 MHz, have revealed reductions in DA concentrations in the hippocampus, which may result in impairments in cognitive abilities such as learning and memory. For example, rats exposed to a specific absorption rate (SAR) of 0.843 W/kg and a power density of 0.02 mW/cm<sup>2</sup> for prolonged periods (ranging from 1 hour daily for several weeks) exhibited significantly lower DA levels in the hippocampus. This decline in DA levels was linked to decreased arousal and impaired learning and memory abilities in the exposed animals. Other studies, including those that involved exposure to 835 MHz RF-EMR, have shown similar reductions in DA concentrations in the striatum, suggesting that EMR exposure may lead to abnormal metabolism of monoamine neurotransmitters in the brain, particularly when exposed to certain intensities of microwave radiation.

### **Effects of EMR on Norepinephrine & Epinephrine**

Furthermore, exposure to EMR is known to affect other crucial neurotransmitters, such as norepinephrine and epinephrine, which are synthesized and secreted by neurons in the brain and adrenal glands. These neurotransmitters play important roles in regulating stress responses, attention, sleep, and autonomic nervous system activity. In some studies, EMR exposure led to a reduction in norepinephrine and epinephrine levels in the brain, with one experiment showing a significant decrease in both of these neurotransmitters in the rat hippocampus after 30 days of continuous exposure to 1,800 MHz microwave radiation. Conversely, other studies have suggested that low-intensity EMR exposure might initially increase norepinephrine levels, but the effects on epinephrine remain inconclusive. The variations in these outcomes highlight the complex nature of EMR's effects on neurotransmitter metabolism and underscore the need for further exploration to clarify the mechanisms involved.

### **Effects of EMR on 5-Hydroxytryptamine "Serotonin"**

In addition to dopamine and norepinephrine, EMR exposure has also been found to alter serotonin (5-HT) levels, a neurotransmitter involved in regulating mood, cognition, and physiological functions such as sleep, pain perception, and body temperature. Serotonin, which is primarily synthesized in the gastrointestinal tract but also plays an important role in the brain, can be disrupted by EMR exposure. Several studies have indicated that microwave radiation leads to significant changes in serotonin metabolism, including increased serotonin turnover and altered concentrations of serotonin metabolites, such as 5-hydroxyindoleacetic acid (5-HIAA). In rats exposed to 900 MHz and 2,450 MHz microwave radiation, the content of serotonin and its metabolites in the cerebral cortex and other brain regions was significantly altered, suggesting a disturbance in serotonin regulation. Furthermore, research has shown that prolonged exposure to EMR, particularly at higher power densities, results in increased serotonin levels in the hippocampus and other brain regions, which may be indicative of a metabolic disorder that

affects the neurotransmitter's functions. These alterations in serotonin levels could contribute to the neurobiological effects of EMR, including mood disorders, sleep disturbances, and cognitive dysfunction.

### **Effects of EMR on Excitatory Amino Acid Neurotransmitters**

Overall, these studies suggest that EMR exposure can lead to significant changes in the metabolism of key neurotransmitters like dopamine, norepinephrine, and serotonin, which are essential for proper brain function. The disruption of these neurotransmitters may contribute to various neurological and psychiatric conditions, including cognitive impairments, emotional disturbances, and other neurobiological effects. The precise mechanisms by which EMR influences neurotransmitter metabolism are still not fully understood, and much of the research conducted so far has been based on animal models. Therefore, further research is needed to explore the long-term effects of EMR exposure on neurotransmitter systems in humans and to determine whether these findings can be directly applied to human health. Furthermore, the complex nature of EMR's effects on neurotransmitter function suggests that more studies are necessary to clarify the specific factors, such as the intensity and duration of exposure, that influence these outcomes. Exposure to electromagnetic radiation (EMR) has been shown to significantly impact both excitatory and inhibitory amino acid neurotransmitters in the brain, potentially causing disturbances in cognitive functions such as learning, memory, and emotional regulation. Glutamate, the primary excitatory neurotransmitter in the central nervous system, plays a crucial role in various brain processes, including memory and synaptic plasticity. It is synthesized from glucose and can also act as a precursor to other neurotransmitters like GABA. Aspartate, another excitatory neurotransmitter, also contributes to excitatory signaling in the brain. Studies have shown that EMR exposure can lead to alterations in glutamate and aspartate levels, with some research reporting a decrease in their concentrations in the hippocampus after acute exposure, suggesting a potential impairment in excitatory signaling. However, other studies indicate that prolonged EMR exposure may lead to an increase in glutamate levels, further complicating the understanding of its effects on neurotransmitter regulation.

### **Effects of EMR on Inhibitory Amino Acid Neurotransmitters**

Moreover, EMR exposure has been linked to changes in the expression of glutamate receptors, particularly N-methyl-D-aspartate receptors (NMDARs), which are essential for synaptic plasticity and learning. Research has demonstrated that EMR exposure can reduce the expression of certain NMDAR subunits, such as NR2A and NR2B, in the hippocampus, potentially contributing to cognitive dysfunction. These findings suggest that EMR may interfere with the normal functioning of glutamate receptors, which could disrupt neural communication and impair memory and learning. On the other hand, inhibitory neurotransmitters like

GABA and glycine also play essential roles in maintaining the balance between excitation and inhibition in the brain. GABA, in particular, regulates various functions such as sleep, emotion, and memory, and its proper functioning is critical for maintaining neural stability. Studies have shown that EMR exposure can lead to a decrease in GABA levels, as well as a reduction in GABA receptor expression, potentially disrupting inhibitory signaling and contributing to an imbalance between excitatory and inhibitory neurotransmission. In addition, long-term exposure to EMR has been associated with increased levels of glycine in certain brain regions, further complicating the effects of EMR on inhibitory neurotransmitters.

In summary, EMR exposure can induce significant changes in both excitatory and inhibitory neurotransmitters, leading to potential disruptions in brain function. These alterations in neurotransmitter metabolism and receptor expression may underlie the cognitive and emotional impairments observed in animal studies following EMR exposure. The precise mechanisms by which EMR affects neurotransmitter systems remain unclear, and further research is needed to fully understand the long-term consequences of EMR on brain health.

#### **Effects of EMR on Acetylcholine (ACH)**

The cholinergic system, particularly the projection arising from the basal forebrain to cortex and hippocampus, plays a critical role in cognitive behavior. One of the key neurotransmitters is acetylcholine. Ach is synthesized from choline and acetyl-CoA under the influence of the enzyme choline acetyltransferase (ChAT) and stored in synaptic vesicles. Excitation of neurons leads to the release of Ach into the synaptic cleft, where it acts on muscarinic and nicotinic receptors to modulate synaptic transmission, learning, and memory. After its action, Ach is hydrolyzed by acetyl cholinesterase to choline and acetic acid. Despite the important role of Ach in cognition, few studies have examined the impact of EMR on its brain metabolism. Various research shows that even exposure to electromagnetic radiation can eventually have implications on Ach synthesis and receptor expressions and cognitive malfunction. Microwaves of 2.45 GHz can transiently rise in brain Ach levels or, after prolonged exposure, alters muscarinic receptor concentrations with simultaneous decline in cognitive functions. Further studies have shown that the exposure of EMR could alter the functional activity of Ach receptors, choline uptake in different regions of the brain, and also disturb the normal balance between Ach synthesis and breakdown enzymes, ChAT and AChE. Besides, evidence from several studies indicates that abnormalities regarding neurotransmitter systems mediated through opioids and NO induced by EMR may take part in cognitive-related deficits. For example, NO acts as a retrograde messenger in synaptic plasticity, and high concentrations of NO, after exposure to EMR, have been related to neuronal injury and learning impairment. The precise modes of these alterations are not known, but studies on the electrophysiological level have pointed to

possible changes in the electrical activity of the brain and in neuronal excitability. While increased cortical excitability, altered blood oxygen utilization, and disrupted sleep patterns during EMR exposure have also been reported, which would support a modulation of neurotransmission-thus accounting for the observed changes in neurotransmitter levels and cognitive performance-in fact, evidence is provided that an interaction between EMR and neurotransmitter systems, especially cholinergic, opioid, and NO systems, constitutes an important key for explaining the cognitive dysfunction induced by EMR.

#### **Cell Membrane Damage**

Evidence shows that EMR considerably affects cell membranes, which are the first and major target of EMF in cells. The implications for such membrane effects include altered neurotransmitter activity in the brain. Thus, understanding how EMR alters cellular processes is very crucial. One of the major ways that EMR affects cells includes changes in membrane permeability, especially about calcium ions. Besides, calcium is also a very crucial signaling molecule inside the cell, and any disruption in calcium homeostasis extends far-reaching effects on cellular processes. Several studies have established that EMR exposure affects calcium channels and/or receptors, hence altering the transport of calcium ions across the plasma membrane, impacting neurotransmitter release and other signal cascades. For example, EMR exposure can increase the number of open calcium channels, leading to an increase in intracellular calcium levels that can disrupt synaptic activity or even cause neuronal apoptosis. This disturbance in calcium signaling may contribute to altered neurotransmission and impair processes such as learning and memory. Besides, VGCCs have been reported to be opened by EMR, leading to very rapid rises in intracellular calcium, NO, and proximities. All of these have been shown to play roles in producing oxidative stress and damage to cells. Recent research into the effects of specific microwave frequencies, such as 2.856 GHz pulsed radiation, has however indicated a depression in cellular calcium levels and would seem to suggest that the influence of EMR upon calcium flux may indeed be related to the type and duration of exposure.

#### **Abnormal Signal Transduction**

Besides the changes in calcium signaling, one more effect of the exposure to EMR is the induction of oxidative stress due to the increased production of ROS, especially in neurons. Neurons are especially sensitive to oxidative stress because most of their energy supply depends on oxidative phosphorylation. The oxidative stress produced by the exposure to EMR results in the disruption of the brain's oxidant-antioxidant equilibrium, enhancing the levels of ROS, which include NO and superoxide; further, proximities is produced. This action precipitates multiple inflammatory pathways, which include NF-kappa B, a signaling pathway implicated in synaptic plasticity, memory, and neuronal protection. This might result in an activation of the apoptotic pathways

after a longer exposure to EMR, which can lead to neuronal death and dysfunction. In the case of DNA damage caused by exposure to EMR, the generation of ROS is considered a key factor because non-ionizing radiation lacks the energy to break chemical bonds directly. The basic mechanism behind DNA damage caused by EMR is oxidative stress due to the production of ROS. Some experimental studies using animals demonstrated that even long-term or relatively brief exposure to non-thermal EMR (900 MHz, 2.45 GHz) could result in neuronal apoptosis. The most sensitive areas include the hippocampus and the cerebellum. It is also said to alter the function of the mitogen-activated protein kinase cascade-a route which is important in regulating many cellular events: metabolism, survival, and proliferation. ROS act as second messengers in intracellular processes, including protein phosphorylation and the regulation of calcium homeostasis. Events that may further activate various pathways involved in a variety of physiological responses after EMR exposure include MAPK and NF- $\kappa$ B, altered neurotransmitter levels, neuronal dysfunction leading to cognitive deficits, and neurodegenerative diseases.

#### **The Influence of RF-EMR on The Modulation of Various Neurotransmitter Levels In The Brain.**

RF-EMR exposure may importantly alter the levels of various neurotransmitters in many regions of the brain. Since various brain regions function interactively and the activity of behaviors involves the interaction of these regions through neurotransmitters, such modulatory effects of RF-EMR will be crucially important. Various studies have pointed out the relationship between RF-EMR and the incidence of amino acid neurotransmitter imbalances in animals and humans. For instance, such imbalances have been reported in studies conducted on young and adult rats (Noor et al., 2011) and humans (Ferreri et al., 2006). In fetal rats, short-term cell phone radiation increased the levels of norepinephrine and dopamine, while longer-term exposure significantly decreased the levels of both neurotransmitters (Jing et al., 2012). Other studies have also reported the disturbance of hypothalamic neurotransmitters (Radwan et al., 2007), thalamic, and striatal neurotransmitters after both short- and long-term RF-EMR exposure. RF-EMR was also shown to alter cortical excitability, which might affect cortical amino acid neurotransmitter levels (Khadrawy et al., 2009). These findings indicate that RF-EMR may have wide and possibly harmful effects on brain chemistry and functions, and further studies are required.

#### **Possible Underlying Mechanism For Structural Changes In The Brain After Rf-Emr Exposure**

These behavioral changes after exposure to RF-EMR may be associated with structural alterations in the brain, especially in specific areas. These may be due directly to the effects of radiation on the brain structures or indirectly through the stress induced by such exposure. A number of mechanisms have been suggested to explain the injurious effects of cell phone RF-EMR on the brain, and these can be grouped into thermal, non-thermal, and cumulative effects. Thermal effects

result from the heating of tissues due to the rotation of polar molecules as induced by electromagnetic fields. This mainly affects superficial structures of the head, with very slight temperature elevation- about 0.1°C on the surface of the head during the use of a mobile phone, according to Tahvanainen, 2007. However, its biological significance is still being debated upon, hence its contribution to the change in brain functions is not yet certain. Less well understood are the so-called non-thermal effects, which involve biological effects unrelated to heating. The non-thermal effects are believed to include changes in neuronal activity, production of free radicals, and interference with intercellular communication. The long-term effects of cumulative damage can lead to greater structural and functional alterations in the brain over time. Knowledge of these mechanisms is important for evaluating the possible risks of RF-EMR exposure to brain health and developing countermeasures to reduce its effects.

#### **Increased Generation of Reactive Oxygen Species (ROS)**

Oxygen-free radicals are implicated in the biological effects induced by mobile phone radiation (Narayanan et al., 2014; Phillips & LeDoux, 1992; DeJullis et al., 2009; Kesari et al., 2012; Alkis et al., 2019). Such, exposure to 900 MHz radiations has been reported to increase the activity of serum superoxide dismutase and to decrease the levels of nitric oxide in animals exposed to radiation. However, no significant changes were observed in NO and MDA levels and the activities of adenosine deaminase, xanthine oxidase, catalase, myeloperoxidase, and glutathione peroxidase both in serum and brain tissues of exposed and control groups (Irmak et al., 2002). In guinea pigs exposed to 890–915 MHz frequency radiation for 30 days, increased MDA levels and decreased glutathione and catalase enzyme activities were reported. However, vitamins A, E, and D3 did not show any altered levels in brain tissues. On the other hand, the levels of these vitamins in blood, as well as MDA and catalase activity, were increased, whereas glutathione levels were decreased (Meral et al., 2007). Neurons require a high amount of oxidative phosphorylation to produce energy; this makes them more susceptible to oxidative stress than other cells. The high metabolic activity and oxygen demand within the brain facilitate the generation of ROS. About 2% of the oxygen is converted into hydrogen peroxide and superoxide anion radicals (de Moura et al., 2010). RF-EMR exposure disrupts the oxidant-antioxidant balance in the brain and may induce oxidative stress. This cascade may be responsible for structural and behavioral alterations over a period of time. The oxidative stress induced by RF-EMR raises several concerns, including:

Interference with learning and memory processes (Alzoubi et al., 2013).

Acceleration of neurodegenerative diseases (Fridovich, 1999).

Promotion of anxiety-like behaviors (Hovatta et al., 2005).

Damage to and oxidation of biomolecules such as sugars, proteins, lipids, and DNA, potentially causing cellular

dysfunction and death (Mohsenzadegan & Mirshafiey, 2012).

Potential tumor-promoting effects (Kamendulis et al., 1999; Aravalli et al., 2013).

These findings underscore the need for further research to fully understand the mechanisms and consequences of RF-EMR-induced oxidative stress.

### Activation of Apoptotic Pathway

It is a programmed form of cell death or apoptosis that, among other contributing factors, represents one of the major mechanisms of cell death in the brain following RF-EMR exposure. Animal studies have shown that even relatively short-term exposure to radio-frequency (GSM 1900 MHz) for 2 hr upregulates components of the apoptotic pathways in neurons, which are more sensitive to this effect compared with glial cells (Zhao et al., 2007). In another experiment, 900 MHz radiation caused apoptosis in rat neuronal cultures through the action of apoptosis-inducing factors (Joubert et al., 2008). Similarly, Maskey et al. (2010) found apoptosis in the CA1 and CA3 regions of the hippocampus and the dentate gyrus in mice; with marked changes in pyramidal neurons after one month of exposure, which may indicate the possibility of impacts on the viability of hippocampal cells. Further research by Ertlav et al. (2018) showed that

RF-EMR exposure at 900 and 1800 MHz increased TRPV1 channel currents, intracellular calcium influx ( $Ca^{2+}$ ), ROS production, mitochondrial membrane depolarization, apoptosis, and caspase-3 and -9 activities in the hippocampus and dorsal root ganglion. Similarly, Kesari et al. (2010) reported DNA damage in rat brain cells after 35 days of exposure to 2.45 GHz radiation. The effects of RF-EMR at the cellular level in humans have also been recorded, and evidence shows its potential to induce apoptosis through signal transduction pathways activated by DNA damage due to radiation penetration (Aitken et al., 2005; Tice et al., 2002). Indeed, increased ROS generation following RF-EMR exposure appears to be one of the major mechanisms driving such apoptotic effects. This brings into light the long-term implications of RF-EMR exposure on neuronal integrity and subsequent brain function.

Various studies have reviewed the impact of exposure to EMR through neurotransmitters in the brain, categorizing its effects according to the duration of such an effect. These studies have fallen between groups that involve either a short-term period-less than one week-or a long-term period-more than one week. A review of the literature indeed does not show significant differences in changes to neurotransmitters between the groups exposed for the short-term and those for

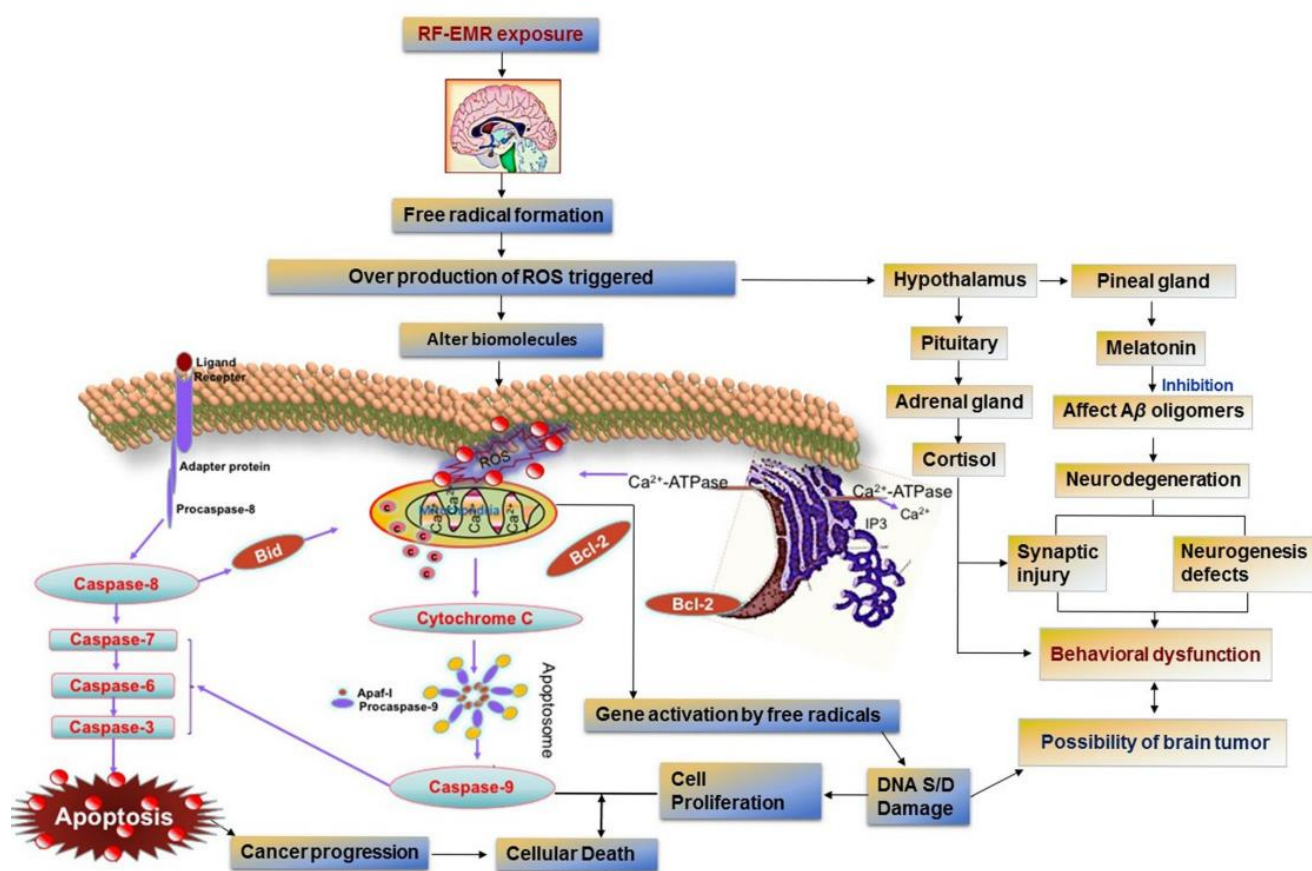


Fig. 4. Potential pathways contributing to behavioral impairments and other biological effects in the brain due to RF-EMR exposure. [45]

the long term. The response to non-thermal EMR is well known to be dependent on factors such as power density and duration of exposure. While some studies report no effects under short-term exposure, this does not necessarily mean that longer-term exposure is without impact. A recent review by Leach et al. considered over 2,600 papers and noted that biological effects were three times more likely to be reported than no effect, suggesting that the outcomes can be very different. The discrepancies in this set of studies could be because of variations in the methodology of experimentation, exposure parameters, and lack of replication between studies. That is why the general literature review is a bit difficult to conduct and compare the results across the studies. Furthermore, although animal models provide insightful information, their complete translation in terms of human health risks is not possible yet, since the conversion rules between animal and human biological effects have not been clearly defined. The establishment of reliable safety standards requires the consideration of various factors like power density, dose, and duration of exposure in order to safeguard against the possible health risks from non-thermal EMR exposure.

A growing body of evidence is available that shows the ability of EMR to induce changes in the calcium function of cells, although specific mechanisms of the effects are not yet resolved. These theories suggest that the change in protein conformation results from an initial activation of calcium, followed by the generation of ROS and finally activation of the molecular pathways of apoptosis. For instance, Lushchak et al. showed that EMR exposure can initially produce free radicals in the brain, which then get converted into ROS. Increased levels of ROS can damage all types of biomolecules inside the cell and, further, can cause calcium release. This may activate genetic factors, leading to DNA damage and, potentially, neuronal apoptosis. The gene expression and levels of enzymes involved might be changed further to activate the downstream signaling pathways, including the mitochondria-dependent caspase-3 pathway of cell death. In summary, intracellular calcium levels and ROS formation are increased by exposure to EMR; both contribute to changes in cellular function and a range of biological effects, including neurotransmitter imbalance. Though important, the integrated effect of these neurotransmitters across various brain regions is also to be considered. Indeed, the change in neurotransmitter levels, if any reported after EMR exposure, may be due to an integrated effect in various areas of the brain: altered neurophysiological states, increased calcium and ROS, membrane damage of the cell, and further changes in signaling downstream. This imbalance between neuronal excitation and inhibition, mediated by neurotransmitter levels, is the cause of the alteration in behavior without any conspicuous change in structure. Neurochemical mechanisms underlying EMR exposure are not well documented, and further research is needed to develop a clearer vision of how EMR actually affects the brain.

## Reproductive Health in Human

A significant number of couples are already suffering from reproductive disorders. The success of pregnancies, as well as offspring health, has been linked with the genetic quality of both partners. An electromagnetic field (EMF) consists of an electric and a magnetic field, and both components are relevant in analyzing exposure. A wave is an electromagnetic radiation with oscillating electric and magnetic fields propagating through space at the speed of light. These waves span from high-energy cosmic rays and gamma rays, at frequencies as high as  $10^{14}$  Hz, to low-energy microwave and radio waves, at frequencies as low as 10 GHz and 100 MHz, respectively, thereby creating an electromagnetic field. These forms of energy have the potential to affect living organisms, although the extent of their impact is not fully documented. There have been many reports in recent years regarding the potential beneficial and detrimental effects of radiofrequency exposure on human health. The energy of electromagnetic radiation is deposited in living tissue and converted to kinetic energy within the tissue particles. The energy absorption in the living tissues can cause an elevation of body temperature, which in high-frequency fields is indeed very possible. In usual conditions, an absorbed value of 4 W/kg of SAR leads to an increase in temperature by 1°C in a healthy individual. Studies have indicated that this does not pose adverse health effects. SAR limits are the basic restrictions, meaning these values should not be exceeded under any conditions. International safety guidelines, to which those of Poland also belong, are based on the idea that by limiting the value of SAR to 0.4 W/kg for the whole body, a sufficient safety margin is ensured for occupational exposure. In the case of the general population, an additional safety factor of 5 is used, and consequently, the limit of 0.8 W/kg was established. While limiting whole-body SAR is important, that does not fully protect against local energy absorption that could lead to localized overheating. Therefore, limits on locally absorbed SAR values are also established. An approach to the analysis of the SAR coefficient is the so-called Finite Difference Time Domain method, which consists in making a discrete model of the object studied and then solving Maxwell's equations in the time domain for the model thus obtained [46].

According to Polish regulations, maximum permissible values of electric and magnetic field strengths at 50 Hz and in the frequency range from 0.001 to 300 MHz, and power densities within the 0.3-300 GHz frequency range, are specified. In areas where the average microwave power density exceeds 0.1 W/m<sup>2</sup> within the 0.3–300 GHz range, human presence is forbidden, except for workers involved in the operation of the field. In residential areas, the electric field strength at 50 Hz should not exceed 1 kV/m, including an institution such as hospitals, nurseries, kindergartens, and boarding houses. Depending on the frequency of the electromagnetic radiation, the magnitude of SAR values induced in humans vary. The electromagnetic wave acts on human reproduction through interference with the male and female reproductive systems and damage to the developing embryo and fetus. Although knowledge about these effects

is still developing, the full scope of reproductive effects remains unclear. In order to conduct studies related to EMF and EMR, peer-reviewed literature and data obtained from an electronic database, PubMed, through various key term combinations, such as electromagnetic field, electric, magnetic, reproductive outcome, semen, and infertility, were used to locate relevant English-language research regarding the impact of electromagnetic waves on human reproduction.

### **EMR and the Male Reproductive System**

The male reproductive system is particularly sensitive to external influences, since sperm does not have the ability to repair genetic material and thus is easily damaged by external factors. Literature concerning the effects of electromagnetic waves on male reproductive cells has shown conflicting results. Some of these studies focus on the duration of phone calls, for example; however, they did not take into consideration life differences or job-related factors in subjects reporting long exposure to GSM frequencies. Thus, the influence of electromagnetic radiation may not act as the primary cause but rather the work environment and high levels of stress. Other studies have researched sperm exposed to specific frequencies outside the body, which, while excluding other influencing factors, do not represent the *in vivo* conditions.

Agarwal et al. have shown that electromagnetic radiation causes oxidative stress, which impairs sperm mitochondria and activates NADH oxidase in the cellular membrane [47]. This results in reduced sperm motility and an inability to fertilize an egg. Disturbances in the redox system led to lipid peroxidation and free radical-induced oxidation of unsaturated fatty acids in the cell membrane. Oxidative stress also disrupts sperm chromatin, increasing its fragmentation and facilitating DNA adduct formation. Impairments in the redox system and ion channel functions contribute to sperm hyperactivation. It has been reported that superoxide radical anions can induce hyperactivation and capacitation of sperm, which is necessary for fertilization of the egg. Capacitation is associated with profound changes in sperm metabolism, including cell membrane changes, which are necessary for the sperm to interact with the corona radiata and zona pellucida of the ovum. Hyperactivation is a transition from symmetrical movements to asymmetrical flagellar beats; this change is necessary for the sperm to penetrate the zona pellucida. Premature capacitation depletes sperm energy and reduces fertilization potential, while the timing of capacitation is regulated by the redox system's homeostasis [48]. This process involves ion transport channels, such as CatSper, pH-regulated calcium-selective channels, KSper (Slo3), and Hv1, which are critical for sperm maturation and fertilization. Mutations in these ion channels are linked to male infertility [49], [50]. Among these, Hv1 is a key channel involved in intracellular alkalization during capacitation and sperm motility and particularly sensitive to electromagnetic waves [51], [52]. Studies have also shown that immune cells are affected by EMR, which modifies calcium ion transport. A similar effect may occur in sperm exposed to electromagnetic waves, and studies on radar radiation as well

as welding arcs both sources of significant electromagnetic exposure--have demonstrated this effect. Exposure to welding radiation, including thermal and ultraviolet light, has been found to decrease sperm motility and increase miscarriage rates in female partners of welders [53]. The studies on radar exposure have given mixed results; while some have shown a reduction in sperm quality, others have not reported any significant effects [54].

**Thermal effects of cell phone radiation:** The regulation of testicular temperature primarily relies on surface conduction rather than blood flow, making it particularly susceptible to the thermal effects of RF-EMW [55]. Given its superficial position, the testis is more likely to absorb EMW energy compared to deeper organs. Physiologically, human testes require a temperature about 2°C below core body temperature to ensure optimal spermatogenesis, and any elevation in testicular temperature can temporarily impair sperm production [56], [57]. Some studies have shown that acute exposure to EMW may directly affect the seminiferous tubular epithelium by increasing testicular temperature [58], [59], [60]. Histological alterations in the seminiferous tubular epithelium, as well as adverse changes in semen parameters such as sperm count and morphology, were found in the experiments with mice exposed to 2.45 GHz (30 W/kg), 1.7 GHz (50 mW/cm<sup>2</sup>), and 2.45 GHz (44 W/kg), respectively. However, the values of EMW energy in these studies are much more compared to the values of energy from modern cell phones. Recent studies indicate that the EMW from commercial cell phones does not have a thermal impact, especially when the value of SAR is less than 2 W/kg [61], [62]. It is considered that a temperature increase by 1°C should require a value of more than 4 W/kg. In one such study, Yan et al. measured the surface and core body temperatures of rats using highly sensitive electronic probes near the face and rectum. They did not find any significant difference in mean face temperature between the experimental group exposed to cell phone radiation at an SAR of 1.80 W/kg for six hours and the control group. Similarly, rectal temperatures remained practically the same in both groups [63]. There is, therefore, no conclusive evidence at present that supports the fact that the radiation from cell phones has a major thermal effect on the human body.

**Non-thermal effects of cell phone radiation:** This process is still under research and involves several metabolic pathways, among which oxidative stress has been recognized as the main mediator. However, the direct action of RF-EMW has also been postulated.

### **EMR and Female Reproductive Health**

Electromagnetic waves affect female reproductive functions similar to their influences on the male system, with the primary putative underlying mechanisms being due to oxidant stress interfering with the ion channel and protein architecture in oocytes, the embryo, and tissues. Because of the anatomy, thermal influences are much more pronounced for the testes than in ovaries. Due to various technical and ethical issues in obtaining oocytes from

humans, most research has been performed using animal models. Gul et al. reported reduced production of ovulatory follicles in female rats exposed to 900 MHz radiation; on the other hand, Roshangar et al. reported structural changes in oocytes, including shrinkage of nucleus and thinning of zona pellucida, and lipid accumulation in the cytoplasm [64]. These were accompanied by manifestations of apoptosis among the granulosa and corona radiata cells. Similar results had been obtained in mouse oocyte and *Drosophila* egg studies, where the effects of electromagnetic radiation had been shown to increase DNA fragmentation and manifest signs of apoptosis [65]. The impact of EMR on embryos has also been explored, and there is some evidence to believe that exposure to certain frequencies hastens DNA fragmentation and developmental disruption. For instance, Borhani et al. showed higher DNA fragmentation in mouse blastomeres exposed to 50 Hz electromagnetic fields, and teratogenic effects were observed in hen embryos exposed to frequencies between 100–1000 Hz by Delgado et al.

Studies investigating the effects of low-frequency (10–50 Hz) EMR exposure have also uncovered various positive findings, such as increased motility in spermatozoa [66]. However, more studies will be required concerning its effects on human reproduction since data about its long-term consequences, particularly epigenetic effects, has not been ascertained. There are studies that look into pregnancy and the impact of electromagnetic radiation upon it. Research indicates exposure, especially to GSM frequencies, may affect pregnancy outcomes and modify placental function in women. Research by Łopucki et al. demonstrated, in placental tissue and cells exposed to 50 Hz electromagnetic fields, morphological changes and increased apoptosis, with modifications in the secretion of calcium ions that can interfere with placental function [67].

#### 4- Conclusion

RF-EMR is a form of nonionizing radiation that does not have the energy to destroy biological structures directly. However, it impressively and importantly acts on the human nervous system. Although RF-EMR itself does not act by ionizing molecules, the exposure to it can further bring about thermal effects at higher frequencies whereby raised temperature of the tissue may have an impact on cellular processes. Other than thermal effects, RF-EMR exposure can cause non-thermal biological responses through mechanisms such as oxidative stress, altered neurotransmitter activity, and changes in the flux of calcium ions within neurons. These cellular disruptions can lead to neuronal apoptosis, which hampers appropriate brain function and can potentially affect cognition and behavior. While the effects on human health are still debated, it is evident that the nervous system, given its sensitivity to electromagnetic disturbances, may be vulnerable to prolonged exposure. While radiofrequency electromagnetic radiation from Wi-Fi, for example, does involve much smaller power compared with mobile phones, and exposure is much farther from the body, there remains considerable ignorance regarding its long-term outcomes,

particularly to sensitive populations of children and teenagers.

While various studies have tended to address a number of questions about RF-EMR risk, especially for brain function and reproductive health, current evidence remains conflicting and thus has necessitated further detailed investigation. It is not possible to decide on a definite conclusion because of the complexity of the biological systems implicated and the difficulty in extrapolating from animal models to human health. However, while neutral or even positive effects can be envisaged at specific levels of RF-EMR exposure, particularly in medical uses, there is still concern about possible risks that may occur above threshold values, particularly in the nervous and reproductive systems. These are potentially very disruptive to neurotransmitter functions, neuronal health, and even sperm and egg cell integrity. Larger, more comprehensive, long-term studies are urgently needed to ascertain the level of exposure that is not harmful and for a full understanding of all biological effects. In summary, exposure to RF-EMR continues to increase with each new generation of technology, including 5G. It is, therefore, of crucial importance that accurate safety guidelines and regulatory frameworks are updated. Continued research into the possible health risks, in particular the cumulative effects of long-term exposure, is essential to safeguarding public health, especially for the younger generation who are exposed more frequently and for longer periods.

#### 5- Future Researches

Longitudinal designs are indispensable, given the rarity of long-term studies on RF-EMR exposure; therefore, future studies should move in the direction of longitudinal designs to investigate chronic RF exposure from mobile phones and Wi-Fi in relation to neurological health. RF-EMR is everywhere in our life; thus, there is an urgent need for research into its cumulative impact on the brain and nervous system. Advanced neuroimaging techniques, like functional MRI and positron emission tomography, provide great opportunities to observe changes in both brain activity and morphology over a certain period. Such tools will enable a research study to compare effects of long-time exposure on brain function and anatomy. Further research into the neurobiological mechanisms of RF-induced changes, including the flux of calcium ions, neurotransmitter functions, and the permeability of the blood-brain barrier, would explain fully the risks posed by RF exposure. Knowledge of these mechanisms is very useful in setting limits of safety and in pointing out potential neurological hazards. Investigation of the RF-EMR effects in the vulnerable stages of life is another promising area. It would also be likely that children's developing brains, adolescents' maturing brains, and the aged brains of older persons all show differential responses to RF. Further studies into the effects of RF-EMR interaction during the sensitivity periods of the development could even specify whether it interferes with RF when normal processes related to brain maturity are taking place. Moreover, studies regarding the impact of RF-EMR on elderly individuals-especially those who are suffering from neurodegenerative diseases like Alzheimer's or Parkinson's

disease-will determine if these types of exposures increase the chances of developing such neurodegenerative diseases. Conversely, novel research in the application of controlled RF exposure could eventually offer new therapeutic routes for neurological disorders.

While much of the current focus has been on the adverse biological effects of RF-EMR, certain frequencies and modulations may hold promise for neurostimulation. Targeted RF treatments could help induce neural plasticity, promoting recovery from brain injuries or cognitive disabilities. Precise modulation techniques and optimization of exposure parameters could lead to new pathways in neurotherapy and non-invasive treatments for a range of neurological conditions. The translation of the results of these studies using animal models still faces many challenges, so their generalization to a population has to be taken cautiously. While changes in behavioral patterns have been noted in rodents exposed to RF-EMR, additional studies will be necessary to explain these changes regarding their impact on human health. With the wide utilization of mobile phones, especially by adults, who spend 4 to 5 hours a day on them, and the increasing usage among teenagers, understanding the behavioral, psychological, and health effects of RF-EMR exposure is important. Such research should also be conducted in respect to critical periods of neurological development and again in older age to better understand possible long-term effects caused by RF-EMR exposure. Given the rapid growth in mobile technology, studies on health risks from chronic RF-EMR exposure should be prioritized, and further investigation is needed to understand how RF-EMR might affect cognitive function, behavior, and overall brain health.

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