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Possible Effects of Electromagnetic waves on Different Systems

Abeer A. Khalefa, Nawal K. Gerges, Hend M. Eissa, Eman R. Abozaid

Medical Physiology Department, Faculty of Medicine, Zagazig University

*Corresponding Author : Hend M. Eissa

hendeissa458@gmail.com, hmeliwa@medicine.zu.edu.eg

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Abstract: EMR is emitted by many natural and manmade sources that play important roles in daily life. Lifetime exposure to EMR is becoming the subject of significant scientific investigation since it has the potential to cause several changes and harmful effects in biological systems. A large body of literature exists on the response of tissues to electromagnetic fields, primarily in the extremely-low-frequency (ELF) and microwave-frequency ranges. In general, the reported effects of radiofrequency (RF) radiation on tissue and organ systems have been attributed to thermal interactions, although the existence of nonthermal effects at low field intensities is still a subject of active investigation. This chapter summarizes reported RF effects on major physiological systems and provides estimates of the threshold specific absorption rates (SARs) required to produce such effects. Organ and tissue responses to ELF fields and attempts to characterize field thresholds are also summarized. The relevance of these findings to the possible association of health effects with exposure to RF fields from GWEN antennas is assessed

Keywords: *Electromagnetic waves*

1. Introduction

EMR is emitted by many natural and manmade sources that play important roles in daily life. Lifetime exposure to EMR is becoming the subject of significant scientific investigation since it has the potential to cause several changes and harmful effects in biological systems **(1)**.

The use of mobile phones and Wi-Fi devices that emit EMR is increasing worldwide at an alarming rate. These devices have improved the quality of life by enhancing data transfer and communication technology. However, powerful energy emitting mobile phones are now commercially available with only limited studies on their hazardous effects on neuronal injury, pain and cancer progression **(2)**.

Cell phones are operating at frequencies between 450 and 2700 MHz. This range is included in radiofrequency field of non-ionizing radiation in which other devices such as Wi-Fi systems, satellite communication systems and TV stations work. The electromagnetic spectrum contains a range of electromagnetic waves increasing in frequency from Extremely Low Frequency and Very Low Frequency (ELF/VLF), through Radio Frequency (RF) and Microwaves (MWs), to Infrared (IR) light, Visible Light, Ultraviolet (UV) light, X-rays and Gamma rays **(3)**.

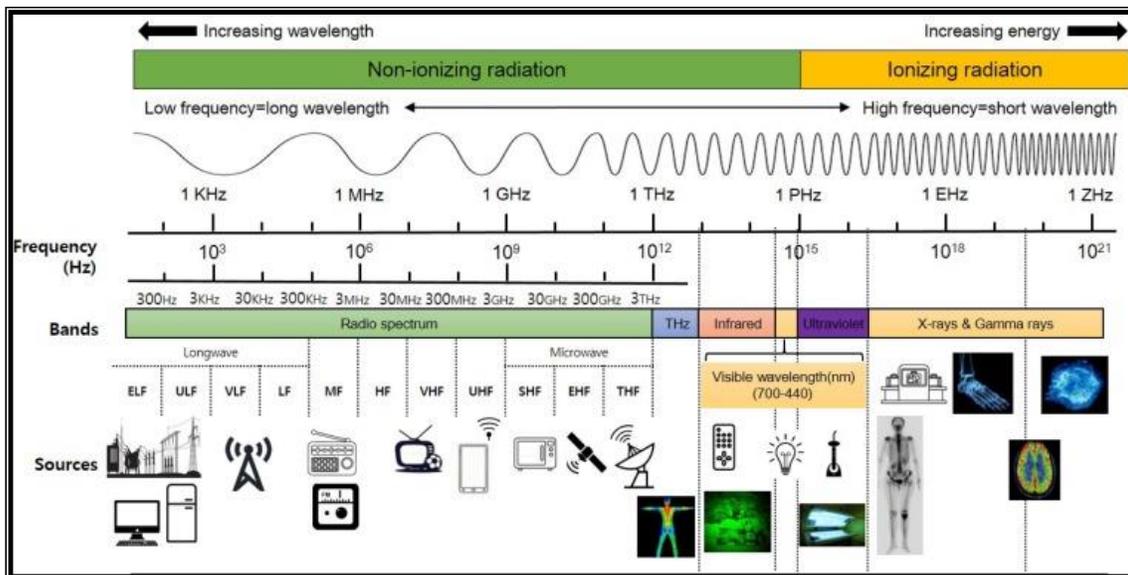


Figure (1): Electromagnetic spectrum. A graphical representation of the spectrum of electromagnetic energy or radiation in ascending frequency (decreasing wavelength) (3).

Effect of EMR on reproduction

A) Effect of EMR on the female reproductive system:

According to many researchers, neuroendocrine changes caused by EMR are a key factor in changing hormone function and causing infertility symptoms in females (4)

During the last decade, studies have shown that long term exposure to EMR have adverse effects on the female reproduction system. The female reproductive system is a set of different parts that are related together. So the effects of this environmental factor must be evaluated on the different parts of the genital system. The female genital system is composed of the uterus, ovaries, fallopian tubes, the released oocysts, and germ & somatic cells in their tissue. Ovaries may be affected more by environmental stressors such as radiation which result in germ cell apoptosis. EMR exposure caused infertility, separation of the thecal layer of primary follicles, irregular thickness in the zona layer and decreased number of ovarian follicles in rats (5).

When rat oocytes were exposed to EMR, they showed shrinking of the nucleus, and their zona pellucida seemed thinner, the number of microvilli was considerably decreased, drops of lipids were observed in their cytoplasm, and the cell organelles were dispersed. In addition, the granular cells and the cells of the corona radiata showed the signs of apoptosis such as condensation of the nucleus, chromatin marginalization and dilatation of the nuclear membrane. Basic morphological changes found in granular cells consisted in their shrinking, atrophy of the microvilli, and atrophy or condensation of the cristas (6)

It had been proposed that the increasing use of electric power may be responsible for the increased incidence of male and female infertility in industrialized countries and an oxidative stress hypothesis had been postulated that EMR-dependent suppression of antioxidant synthesis may be responsible for the stronger increase in infertility (7).

It is well known that EMR-induced injury leads to increased production of ROS. When water, which is a main constituent of cells, is exposed to EMR, ROS occurs through a variety of mechanisms. Although all respiring cells are equipped with protective enzymatic and nonenzymatic antioxidants, increased oxidative stress in cells stemming from EMR overcome the protective systems and cause oxidative depletion of these antioxidants leading to cell injury and apoptosis (7).

Shahin et al. (8) reported that low level 2.45 GHz MW radiation was able to affect implantation and pregnancy via inducing oxidative stress. Their study elucidated that in MW exposed mice implantation sites were affected

significantly when compared to control. It was found that mice exposed to 2.45 GHz at a power density of 30 mW/cm² have shown decreased implantation sites per litter and reduction in fetal weight during 1–6 days of gestation.

Ovulated and mated female mice exposed to 50 Hz EMF for four hours per day, six days a week for two weeks showed decreased number of blastocysts with increase in DNA fragmentation. These findings indicated that EMR exposure in the pre-implantation stage had negative effects on embryonic development. **(9)**

Concerning the use of mobile phones during pregnancy, it had reported that the state of the newborn evaluated directly after delivery according to the APGAR scale, was worse in women exposed to a greater degree to the waves of the EMR. An explanation of this phenomenon may be due to the effect exerted by EMR on the placental functions **(9)**

B) Effect of EMR on the male reproductive system:

The male reproductive system is a group of tissues very sensitive to external factors, and sperm which does not possess the capability of repair of its genetic material, and for this reason seems to be vulnerable to various kinds of damage generated by external factors **(10)**.

Testes in which spermatozoon production takes place are located at a close distance from mobile phones carried in back pocket, front pocket or on waistband. This causes testes to be exposed to EMR waves emitted by mobile phones for long hours during the day. Therefore, the number of studies on the effect of mobile phones on reproductive functions has increased in recent years. In studies carried out on rat models, it has been reported that exposure to mobile phones results in negative histological and morphological alterations in testes **(11)**.

The exposure to 2.45 GHz EMR radiation emitted from WiFi transmitter caused a marked reduction in the weight of epididymis and seminal vesicle without affecting the weight of the testes in rats. Interestingly, the weight of cauda epididymis is positively related to sperm count, sperm maturation and reservoir **(12)**.

Histopathological evaluation on the testes had demonstrated various degenerative features including irregular shape, decrease in diameter of seminiferous tubule, thinning of tunica albuginea layer with dilated and congested blood vessel both in tunica albuginea and in the interstitial space. Ample spaces between the Sertoli cells and spermatogonia and the detachment of spermatogonia from the tunica propria had creates peripheral spaces. These peripheral spaces caused disconnection of Sertoli and spermatogonia interaction. Subsequently, this will cause a decrease in spermatogonia proliferation leading to spermatid density depletion in the seminiferous tubule and therefore reduced sperm count **(4)**

Most of the studies reviewed also demonstrated that Leydig cells were affected as evidenced by a reduced number of cells **(4)** and abnormal irregular appearance **(8)**.

Since testosterone is a very important hormone for spermatogenesis as well as for the maintenance of structural and physiological function of seminiferous tubules decreased levels of this hormone may further exaggerate spermatogenesis impairment following the exposure. Human studies also showed similar findings. Therefore, oxidative stress in male reproductive organs elevated following the exposure to RF-EMR emitted from Wi-Fi transmitters **(13)**.

The resulting oxidative stress could play a pivotal role in the mitochondrial damage causing the loss in sperm motility, one of the most significant causes of fertility impairment. The involvement of both mitochondrial metabolism and oxidative balance can suggest that ELF-EMR could act as an environmental trigger for the intrinsic apoptosis pathway during spermatogenesis **(14)**

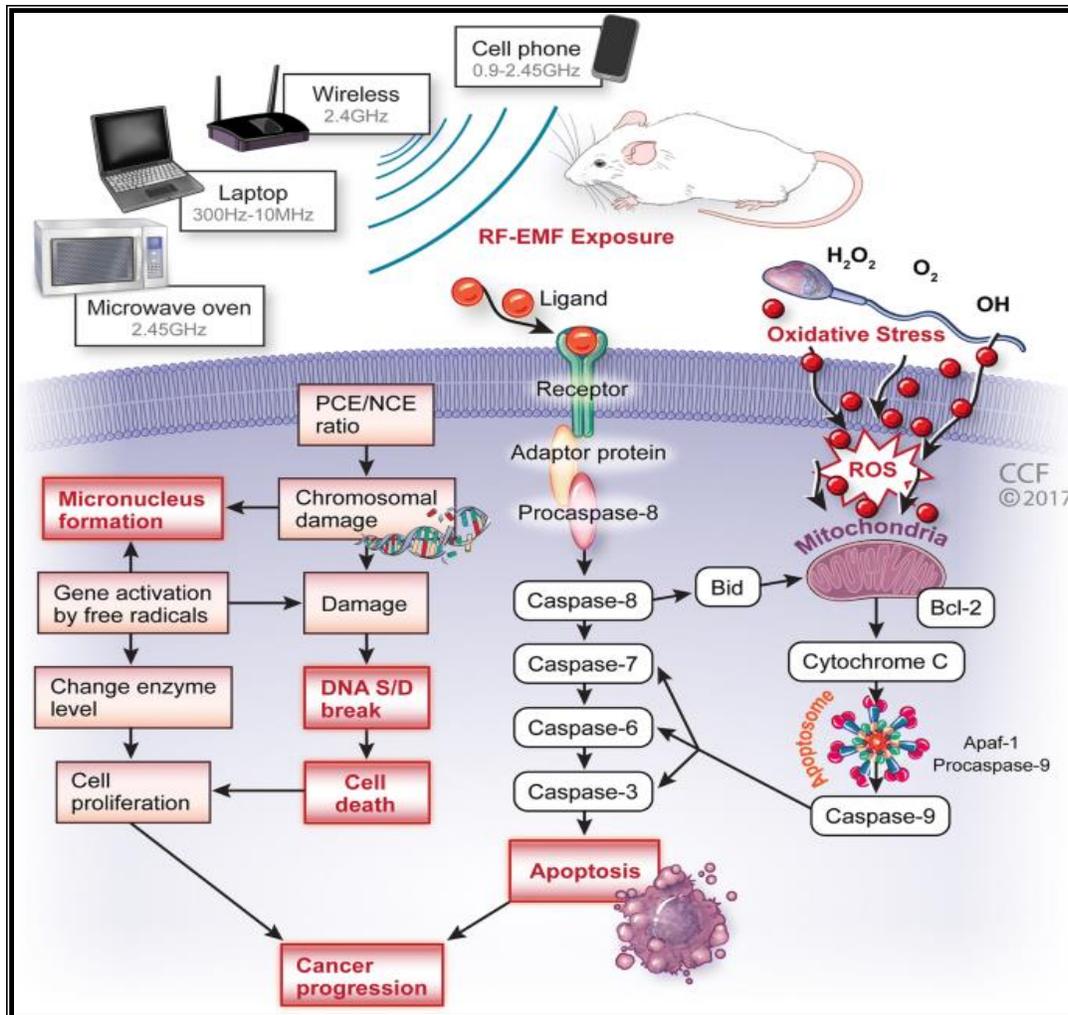


Figure (2): An overview on the effects of EMR exposure, emitting from various sources (cell phone, microwave oven, Wi-Fi, Laptop) on male reproductive system (14)

Effect of EMR on cardiovascular system

In humans, several studies have shown that heart rate variability was altered during acute exposure to EMR from mobile phones, such as an increase in parasympathetic tone, concurrent with a decrease in sympathetic tone. Other studies on the chronic effects of mobile phones in healthy humans have reported a decrease in parasympathetic tone and increase in sympathetic tone. Exposure to EMR altered the CVS function in a rat model, in addition previous studies suggested that long term exposure to EMR generated free radicals such as ROS leading to oxidative stress injury and cardiomyocyte structural alterations in rats (15)

Effect of EMR on Endocrinal glands

Regarding the endocrine system, the sensitivity of pineal gland, pituitary gland, adrenal gland and thyroid gland as well as of the endocrine pancreas to EMR has been investigated. The thyroid gland is one of the most exposed and vital organs and may be a target for any type of EMR. In an investigation of change in thyroid hormones and thyroid stimulating hormone (TSH), decrease T4 concentration and normal level of T3 were observed (16).

Baby et al. (17) found there was a significant correlation between total radiation exposure and an increase in TSH among both groups in those with and without family history of thyroid illness.

Different studies have suggested that EMR exposure may act as a chronic stressor. Over the past decades, researchers have revealed that ELF-MW can act on the anxiety-related behavior of animals and the emotional state of people. The effects of EMR on stress hormones, depression-like states and anxiety-related behaviors have been investigated in many studies and their results are contradictory (18).

Some reports stated that long term ELF-EMF stimulation increases the plasma adreno-cortico-trophic hormone (ACTH) and cortisol levels; however, another study showed that chronic ELF-EMF exposure did not change or significantly decreased the level of both hormones (19).

EMR and cancer:

The association between EMR exposure from mobile phone use and tumor development in the brain and central nervous system has been much investigated. Although many large and well conducted studies have found little evidence to support this association (20)

The International Agency for Research on Cancer (IARC) reevaluated the risk of tumor development in the brain and central nervous system from mobile phone use and rated this type of exposure as a possible human carcinogen (grade 2B) (20)

This declaration was based mainly on the results of two epidemiological studies which were the Interphone study and Swedish study by Hardell and colleagues (20)

Children are considered more vulnerable than adults to environmental exposure including EMR. There is a possible link between leukemia and exposure to EMR. **Hocking and Gordon (21)** studied the incidence of childhood leukemia as a function of the distance from TV transmitters, finding an increased risk of leukemia in children living within a radius of less than 4 km compared with those living in a radius of 4 to 12 km.

Effect of EMR on nervous system:

Effect of EMR on locomotor behavior

Many researchers have reported the effects of EMR on locomotor behavior in animals. According to some of these studies, RF-EMR does not alter the locomotion. But some researchers have shown positive correlation between cell phone radiation and locomotor behavior in rodents (22).

Decreased locomotor activity was observed in rats when exposed to mobile phone radiation (4 h/day) for 15 days. **Obajuluwa et al. (23)** reported that exposure to 2.5 GHz radiations for 4 to 8 weeks of duration reduced locomotor activity in rats indicated by reduced line crossing frequency pattern in open field test. In the meantime, a report by **Narayanan et al. (24)** demonstrated that mobile phone radiation over a period of 1 month did not significantly alter the general locomotion in rats.

Effect of EMR on neurotransmitter levels in the brain

EMR exposure can potentially alter the neurotransmitter levels in various brain regions. Therefore, the modulatory effect of EMR on various neurotransmitter levels in various brain regions is a serious concern. According to many studies, there is a clear relationship between exposure to EMR and amino acid neurotransmitters imbalance in various parts of the brain of young and adult rats and in humans too (25).

Effect of EMR on Electroencephalogram (EEG)

EEG data reflect the functional state of the brain by enlarging the autologous weak bioelectricity recorded by the EEG recording instrument. An abnormal EEG is closely associated with damaged cognitive ability. EEG is often used as a tool to diagnose Alzheimer's disease. Most studies have suggested that microwave radiation can cause EEG abnormalities in experimental animals and participants, but some negative results have also been reported in studies using low-power microwaves (26).

In a study investigating the influence of low frequency microwave 450 MHz radiation on EEG, **Hinrikus et al. (27)** found that MW radiation enhanced brain wave energy, decreased brain wave frequency, and increased the amplitude and power of delta frequency bands, indicating a decrease in learning ability

Suhova et al. (28) exposed volunteers to microwaves at a frequency of 450 MHz for 10 repeated intervals of 1 min of irradiation and 1 min off. The SAR of the two groups were 0.303 W/kg and 0.003 W/kg. A resting eyes-closed electroencephalogram was used to continuously record the results, which showed that

there was an increase in the power of the α , β_1 and β_2 frequency bands in the 0.303 W/kg group and in the β_2 frequency bands in the 0.003 W/kg group.

EMR and memory

Memory can be defined as any physical change that carries information about the historical past. Typically, in animal systems, memory is stored in physical changes inside and between neurons (29).

Memory Categorization:

In neuropsychology, memory is divided into two main categories, declarative and non-declarative memory systems (30).

- I. **Declarative Memory:** it encompasses: episodic memory (memory for events in one's past) and semantic memory (memory for general knowledge) (31).

Declarative memories can be encoded intentionally or unintentionally, but are typically explicitly (i.e., with awareness) accessible by active recall attempts. Integrity of hippocampal circuitry is a prerequisite for retaining an episode as well as spatial and temporal context information in memory for more than 15 min (31).

- II. **Non-Declarative Memory:** in contrast to declarative memories, it can be acquired without involvement of medial temporal lobe structures. Non-declarative memory encompasses quite different memory systems that rely on different areas of the brain. It includes procedural memories for motor skills (motor areas, striatum, cerebellum) and perceptual skills (sensory cortices), certain forms of conditioning and implicit learning (priming), etc. Non-declarative memories can be implicitly (i.e., without awareness) acquired and recalled, and learning is slow, usually requiring multiple training trials (32).

Memory Processes: Memory functions comprise three major sub-processes, i.e., encoding, consolidation, and retrieval.

- a. **Encoding**, the perception of a stimulus results in the formation of a new memory trace, which is initially highly susceptible to disturbing influences and decay, i.e., forgetting (30).
- b. **Consolidation**, the labile memory trace is gradually stabilized possibly involving multiple waves of short and long-term consolidation processes which serve to strengthen and integrate the memory into preexisting knowledge networks (30).
- c. **Retrieval**, the stored memory is accessed and recalled (30).

Activity occurring in the neuronal representation of a memory following encoding is thought to promote two kinds of consolidation processes, termed "synaptic consolidation" and "systems consolidation", referred to as the standard two-stage memory system (33).

Synaptic consolidation leads to the remodeling of the synapses and spines of the neurons contributing to a memory representation, eventually producing changes in the efficacy of the participating synapses (33).

Hippocampal Role in Learning and Memory

Hippocampus is a sea-horse structure embedded deep into temporal lobe. It is divided into hippocampus proper (Cornu ammonis; CA), dentate gyrus (DG), subiculum, and entorhinal area. The entire set is called the hippocampal formation. Hippocampus proper (Cornu ammonis) is divided into CA1, CA2, CA3, and CA4 (34).

Tang et al. (35) reported that exposure to 900 MHz radiation had altered the neurobehavioral performance in rats. These changes were more explicit in 28-day exposed group as demonstrated by impaired spatial memory and damaged blood-brain barrier (BBB) permeability.

Studies had also proven that exposure to 900 MHz radiation can also alter the spatial learning and reference memory and induce morphological changes in the hippocampus CA1 region. In another study, a single 45-min exposure to 900 MHz radiation had induced an elevation in 5-Hydroxy tryptamine (5-HT) level without changing blood glutamate levels of rats. Increased 5-HT level led to learning impairment and spatial memory deficit (36).

Reports also indicate that, chronic mobile phone radiation exposure could severely interact with the consolidation phase of recognition memory in mice and it is postulated that this may be due to the effect of EMR on information transfer pathway connecting the entorhinal and parahippocampal regions as they are involved in the object recognition memory task (36).

Effect of EMR on mood and behavior

Anxiety can be defined as an emotional and physiological response that can influence humans as well as animals, which could be associated with a threat to their well-being (37)

Anxiety-like behavior in animal models is often extrapolated to the anxieties that are reported in human beings. It is considered as a pliable response to a foreign environment, chiefly when the individual is exposed to any alarming situation or threat. Astudy indicates the widespread usage of mobile phones as a proven potential risk factor to human health in this era of technology boom. For investigating anxiety-like behavior in animal models over the years, researchers have developed various behavioral paradigms. Some of the commonly used strategies in testing anxiety in animal models include elevated plus maze (EPM), open field test (OFT), and black and white box (24)

Astudy by Zhang et al. (38), in EMR-exposed mice brain, revealed significant reduction in gamma amino butyric acid (GABA) and aspartic acid in cortex and hippocampus, the authors claim that the possible cause of anxiety in EMR exposed rat brain could be due to the reduction in GABA and aspartic acid. OFT, in EMR-exposed mice, revealed a significant reduction in the time spent and distance traveled in the central arena in comparison with the sham group. This is considered as a behavioral indicator of elevated anxiety levels.

Effect of EMR on Oxidative Stress and inflammatory response:

Regarding the oxidative processes, approximately 1% of the oxygen used in cells is transformed into free radicals (chemical species with an unpaired and highly reactive electron), usually called ROS. The ROS, such as the superoxide anion radical, the hydroxyl radicals, and the non-radical hydrogen peroxide (H₂O₂), are all by-products formed as part of the normal aerobic metabolism of the mitochondria and peroxisomes (39).

Antioxidants are a structural heterogeneous group that share the ability to scavenge free radicals and are the first defense against the potential damage of ROS. One of the most significant endogenous antioxidants is the tripeptide glutathione (GSH), which is oxidized by different radicals into glutathione disulfide and confers protection mainly in highly metabolic tissues. CAT, SOD and GPx are the most studied enzymes in charge of transforming free radicals into more stable chemical forms and constitute the main antioxidant defenses of animals (39).

Oxidative stress is caused by an imbalance between pro-oxidants and antioxidant. This ratio can be altered by increased levels of ROS and/or reactive nitrogen species (RNS), or a decrease in antioxidant defense mechanisms. The brain is rich in polyunsaturated fatty acids and has high metabolic rate which makes it vulnerable to ROS and oxidative damage as compared to other organs of the body (39).

EMR and Apoptosis

Apoptosis is a programmed cell death characterized by a variety of morphological, biochemical, and genetic markers. Apoptosis plays a fundamental role in normal tissue homeostasis during embryogenesis and through the entire life time of multi-cellular organisms. The role of environmental stressors in modulating many cellular functions, such as proliferation and apoptosis, had been formerly documented. (40)

Studies have indicated that two distinct apoptotic pathways are followed in mammalian systems: the extrinsic or death receptor pathway and the intrinsic or mitochondrial pathway. The extrinsic pathway involves binding of death ligands such as TNF- α to their cognate cell surface receptors tumor necrosis factor receptor 1, resulting in the activation of initiator caspase-8 and subsequent activation of effector caspase-3. However, in the intrinsic pathway, cells can respond to various stressful stimuli by triggering apoptosis, through Bax/Bcl-2/Caspase-9 cascade where caspase-9 cleaves and activates the apical effector caspases such as caspase-3. Caspase-3 is thus regarded as one of the key executioners of apoptosis, being responsible either partly or totally for the proteolytic cleavage of many key proteins. In this context, some studies had reported that the induction of caspase-dependent apoptotic pathways was attributable to EMR exposure (41).

Motawi et al. (42) showed that exposure to mobile phone for 60 days (SAR = 1.13 W/kg, 2 h/day) increase active caspase-3 along with an up-regulation of Bax and a down-regulation of Bcl-2 gives evidence of disturbance of the intrinsic apoptotic machinery in rat brain tissue, moreover, the observed increase in TNF- α

level of exposed and activated groups of either young or adult rats pointed to the involvement of the extrinsic pathway as well.

Moreover, **Joubert et al. (43)** observed increased caspase-3-independent apoptosis in rat primary neuronal cultures exposed to a 900-MHz continuous-wave radiofrequency radiation at 2 W/kg for 24 h. On the other hand, in vivo study on rat brain cells suggested a probable effect of electromagnetic field on DNA damage producing single and double-strand breaks and an increase in micronucleus incidence in lymphocytes of workers exposed to EMR. It had been shown that short term exposure to radio-frequency emissions 1900 MHz for 2 h upregulated the elements belonging to apoptotic pathways in neurons. The neurons were more sensitive to this effect than the glial cells **(44)**.

In one of the studies, cultures of rat neurons were exposed to 900 MHz radiation field showed apoptosis with apoptosis-inducing factor **(43)**. But in a study apoptosis was seen in CA1 and CA3 regions of hippocampus and dentate gyrus of mice.

Ertlav et al. (45) have reported that EMR exposure (900 and 1800 MHz) induced increases in transient receptor potential vanilloid 1 (TRPV1) channel currents, intracellular free calcium influx (Ca^{2+}), ROS production, mitochondrial membrane depolarization, apoptosis, and caspase 3 and 9 activities in the hippocampus and dorsal root ganglion of rats.

Kesari et al. (46) have investigated the effect of exposure to 2.45 GHz frequency for 35-day, it affected the DNA of rat brain cells.

Researchers also reported that the signal transduction processes induce apoptosis in response to DNA damage due to deep penetration of radiation in the brain. These are mainly attributed to increased ROS generation following EMR exposure. **(47)**.

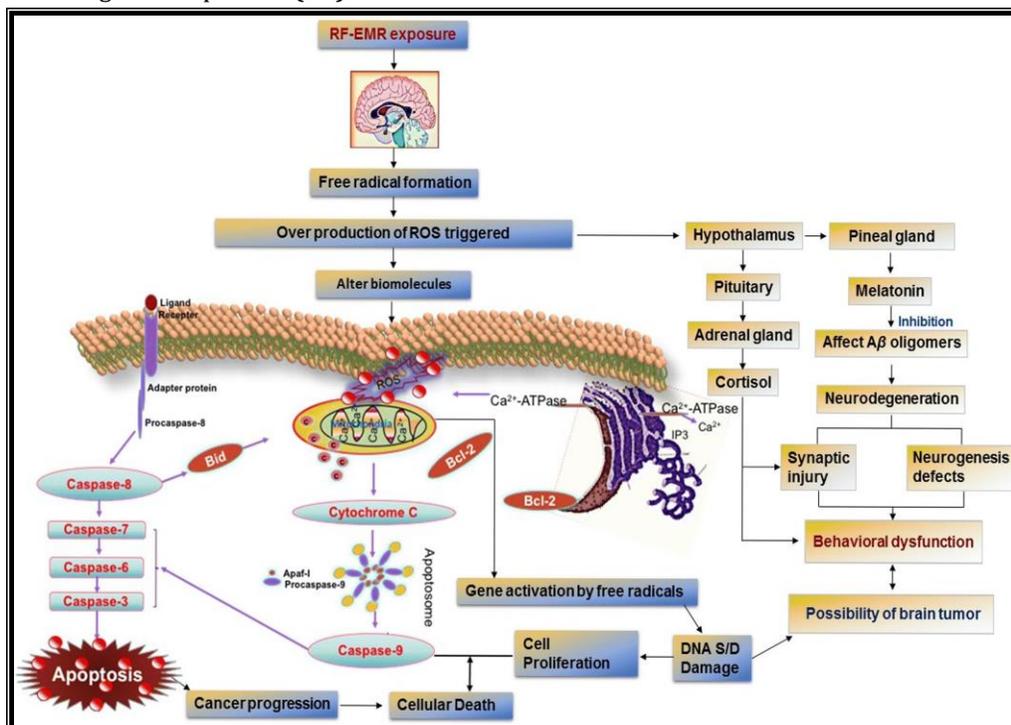


Figure (3): Possible pathways leading to behavioral dysfunction and other biological effects in the brain following RF-EMR exposure. **(47)**.

EMR and CREB

CREB is an important transcription factor that plays an important role in the processes of learning and memory. The phosphorylation of CREB affects the expression or activation of genes and the overall behavior of neurons.

CREB is a key transcription factor that regulates the expression and activity of genes to alter the function of neurons **(48)**.

CREB is also a connection between several neural function-related pathways, the phosphoinositide 3-kinase (PI3K)/Akt strain transforming (AKT) pathway, calcium/calmodulin-dependent protein kinase II (Ca²⁺/CaMKII) pathway and mitogen-activated protein kinase (MEK)/extracellular signal regulated kinase (ERK) pathway are three key upstream pathways of CREB and regulate the expression of multiple downstream functional proteins in the nervous system **(48)**.

The transcriptional activity of CREB depends on its phosphorylation status, which is determined by the opposing actions of protein kinases and phosphatases, phosphorylation is a key mechanism in signaling and has been described to regulate several processes such as the cell cycle, cell death, DNA damage and neurogenesis **(49)**.

For example, increase in intracellular calcium (Ca²⁺) levels through voltage- and ligand-dependent channels results in increased cAMP levels via activation of G-protein-coupled receptors. Growth factors can also activate receptor tyrosine kinases to augment cAMP levels. All these pathways affect CREB phosphorylation levels. Downstream of neuronal activity, the PKA, mitogen-activated protein kinase and Ca²⁺/calmodulin-dependent protein kinase IV (CaMKIV) pathways result in CREB phosphorylation at Ser133. Protein phosphatase-1 and protein phosphatase-2 are the major CREB phosphatases, and Ca²⁺-dependent signals can induce intracellular events that lead to phosphorylation or dephosphorylation. The effect of stimulation depends on the nature of the stimulus and its cellular context. For example, activation of *N*-methyl-D-aspartate (NMDA) receptors leads to CREB dephosphorylation in extrasynaptic neurons, while in synaptic sites, it leads to CREB phosphorylation and CREB-dependent gene expression **(50)**.

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