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Open Access Short Review

Crescent Journal of Medical and Biological Sciences
Vol. 4, No. 3, July 2017, 92–98
eISSN 2148-9696

Probably Role of Antioxidants Against EMFs-Induced Effects on Central Nervous System Structures: A Mini Review

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Abstract

Electric and magnetic fields (EMFs) are one of the main environmental pollutants inducing adverse effects on life quality. Waves emitted from industrial and domestic equipments always expose humans to the risk of some diseases. The central nervous system (CNS) is one of the structures sensitive to these waves, which could be damaged seriously. Complexity of the neural structure demands more researches based on morphological and histological changes. Important factors involved in EMFs effects on neural function concern the type, frequency, intensity of waves and duration of the exposure. Surely, increased dosage of the electromagnetic waves results in severe consequences on the function of brain neurons. However, antioxidants may prevent chronic injuries via different methods. The critical periods of fetal, childhood, or pregnancy are more susceptible to irreparable risks of electric magnetic waves. There are several strategies to reduce effects of such waves, by using antioxidants, for instance. However, different theories have been presented on their efficiency due to the abundance of antioxidants available in nature. In the present review, we conclude that even low-dosages of EMFs would have negative effects on CNS. According to some previous studies, various dosages of antioxidants have different effects on neural function leading to various theories on this subject.

Keywords: Electromagnetic fields, Central nervous system, Antioxidants

Introduction

Humans and animals are always exposed to electric and magnetic fields (EMFs) coming from various diffusion sources, for example, from instruments such as computer devices, television, power lines, radio and telephone communications. Effects of electrical and magnetic devices may depend on the exposed genus, tissue density and the life period. EMFs are non-ionic radiations diffused from one point to another. Many physical energies like ultraviolet, X-ray and sun light are isolated from electromagnetic fields. Various types of EMFs have different characteristics which are usually divided into 4 categories: 1) static types defined by zero frequency, for example, waves released from magnetic resonance imaging (MRI) and geomagnetism (1); 2) Extremely low frequency (ELF-EMF) contains the waves with ≤300 Hz frequency, generated via military equipment and railways; 3) IF-EMFs (intermediate frequency) are frequencies between 300 Hz to 10 MHz, produced by industrial cables, television, and PC monitors; 4) Hyper frequency (HF-EMF) includes frequencies between 10 MHz to 3000 GHz generated via mobile phone and radio antennas. Radio frequencies (RFs) are another type of HF-EMFs with 100 MHz frequency.

Physiological parameters which produce oxidants and antioxidants may be impressed by disturbance factors like EMFs. There are extensive studies on the relationship between EMFs and most abnormal disorders, especially amyotrophic lateral sclerosis (ALS), childhood leukemia, adult brain cancer and miscarriage (2). The EMFs correlation with biological systems relies on the frequency, amplitude, wavelength and polarization (3). Increased EMFs exposure can affect the cellular function by producing reactive oxygen species (ROS) (4). The over production of ROS can destroy cellular ingredients particularly lipids and proteins in membranes and the signal transduction process. Moreover, ROS can damage cells by depleting antioxidants capability leading to genetic mutations (5). The cell cycle changes, induction of apoptosis and mutation of protein expression have been reported (6). ELF-EMFs exposure can fixate free radicals increasing their stability and broad dispersion in cell structures (7). This may result in immune system disorders such as an enhanced super-oxide production in mouse macrophages, human monocytes and rat neutrophils (8). Factors acting on the nervous system can directly or indirectly change physiological parameters such as morphological, chemical, or electrical ones and finally lead to neurological effects. The obvious manifestations effects can be seen in disorder changes including a

Received 18 October 2016, **Accepted** 27 February 2017, **Available online** 4 April 2017

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weak memory, low-levels of learning and consciousness. The nervous system is an electrical structure which any factor like exposure to electromagnetic fields can make neurological alterations. The aim of the present review is to investigate the effects of EMFs on structure and function of central nervous system (CNS) explained in some studies. In addition, some herbal and chemical antioxidants, that may be useful for neural system, are referred in this review.

Material and Methods

Biological Effects of Electric and Magnetic Fields

Exposure to EMFs generates electric flows and magnetic fields that interact with the current-voltage of biological system and affects the physiological homeostasis. If this electric current induces the stimulation threshold, membrane polarization of the nerves and muscles may change. These fields at physiological rates may extend the life-period of free radicals, leading to genetic and molecular damages (9). Several epidemiologic findings have been shown in mammalian populations, experimental rodent animals and cell lineage (10). The biological reflexes to EMFs can usually be explained by two mechanisms including thermal and non-thermal effects (11). Thermal effects are recognized by heat production in the specific site of body and non-thermal effects on absorption rates of the wave's energy without the heat generation. Electromagnetic fields have various impacts on cellular structures, cell differentiation and proliferation (12), DNA and cells chromosome (13), blood flows (14) and the fetus birth (15). In relation to the cardiovascular system (16), bone marrow (16), hormonal and respiratory systems, disorders caused by EMFs in the cell and tissues manners change the activity of these vital systems. According to recent findings, exposure to 2.4 GHz WI-FI increases blood pressure and heart arrhythmia (17). EMFs can also affect endocrine system. Many studies have been conducted on the melatonin and derived tryptophan synthesized by pineal gland (18). It is believed that most of noxious outcomes of EMFs are produced via protein synthesis (19) which decreases enzymes and their catalytic activity. Mainly, the findings of toxicity effects have been studied on critical cells in various organs including fibroblasts of connective tissue, melanocytes of epidermis, lymphocyte of thymus and other lymphatic tissue, monocytes in blood, muscular cells of human and granulosa cells of rodents.

Oxidative stress occurs in unbalanced condition between the generation of free radicals and antioxidant capacity in the body (20). The antioxidant defense systems can be damaged by these waves and lead to increased oxidative stress levels. It has been revealed that the aging process reduces resistance to EMFs pro-oxidant attacks. Therefore, aging people are more sensitive to electromagnetic waves. ELF-EMF is a main factor causing a significant decrease in antioxidant enzymatic valence among young and adult rat brains (21,22).

Particularly in rats' brains, exposure to 50 Hz of ELF was reported to induce a noxious toxicology effect through impairing the catalase (CAT) antioxidant defense. Moreover, a combination of movement contraction and vigorous lipid peroxidation and impairment of CAT activity in Wistar rats' brains due to chronic exposure to ELF-EMFs has been observed (23).

Non-thermal effects are related to the production levels of oxidative stress and also to penetration of the blood-brain barrier, which is manifested by alterations in encephalogram and blood pressure (22). Oxidative stress has been suggested as the fundamental mechanism responsible for RF type effects. It has also been confirmed that RF-EMFs produce extracellular ROS through agitation of the cell membrane in vitro (24). In a study in 2006, an increased production of ROS after exposure to RF-EMFs was also reported in rats' lymphocytes (24). Another study in 2010 showed that decreased activity of superoxide dismutase (SOD), myeloperoxidase (MPO) and glutathione peroxidase (GSH-Px), as the result of exposure to RF-EMFs, led to lipid peroxidation in rat kidney and guinea pigs liver (25,26). However, there were no remarkable ROS levels in human cell lines (auditory hair cells) after being exposed to RF-EMFs (27). Although free radicals are required for vital processes, particularly for brain metabolism, ELF-EMFs may extend duration and concentration of free radicals in living cells. In fact, ELF-EMFs are among the main factors that increase free radicals content with lipid oxidative detriment in mice and rats' brains.

Results

Electric and Magnetic Fields and Neural Diseases

Destructive physiological effects through oxidative stress result in conditions which cause homeostasis dysfunction. It has been confirmed that free radicals can have an impact on gene regulation in cells, mainly DNA mutation, and finally promote carcinogenesis (28). But according to a supplementary view of free radicals and stress oxidative, those factors are able to create neuropathological conditions such as Parkinson disease (PD) and Alzheimer disease (AD) (29). Although there are numerous studies on the relationship between EMFs and neurodegeneration, the experimental detections are still controversial and rely on both characteristic properties of EMFs and various causes of diseases. EMFs may be detrimental or protective in neuronal response depending on the dosage, frequency and exposure period. They even have some applications in medical therapies. Unfortunately, there is no univocal explanation of the EMFs effects on brain and neural degeneration. The impact of RF on physiological systems has been a topic of intense argument. Recently, this issue has been highlighted due to the modern utilities of RF-EMFs in several radio electrical devices, such as cordless stationary phones and wireless computer communication. It has been suggested that only the waves absorbed from RF-EMFs can affect physiological systems. A high-level radiation changes thermal energy rate in the biological system and this is responsible for most of the causes

observed in acute or chronic effects. However, it is now admitted that even low-level EMF exposure without inducing thermal effects would have a biological response. Therefore, the designation of non-thermal effects and recognition of them from thermal effects are considered as the main obstacle. The oxidative stress can be one of the probable assumptions on non-thermal effect of RF-EMFs; albeit, experimental detections were incompatible with pro-oxidant capability of GSM exposure in primary cortical neurons cultures in brain, and no effect had been observed in human neuroblastoma and mouse fibroblasts (30). Such inconsistencies in neuronal parameters in response to RF reveal indeterminacy in identifying the molecular impacts by GSM and discriminating thermal from non-thermal effects. In 2010, Arendash et al indicated that longer exposures to RF improve cognition in AD animals, which indicates a potential noninvasive and non-drugged strategy in treating AD (31). Another report in 2012 showed a down regulation of α-synuclein in cortical cell culture of rat embryos' brain by low SAR GSM-900 MHz exposure (30). In AD models, researchers have demonstrated that all the cognitive advantages of RF waves can be achieved without increasing the brain hyperthermia and oxidative stress (31). Furthermore, the experimental findings on long term RF effects and the brain mitochondrial function of animals' AD transgenic (Tg) (32) have shown a decreased ROS production and increased mitochondrial membrane potential in their hippocampus and cerebral cortex. There are diverse studies on human and animal subjects, which have reported the following electromagnetic effects: Reduction in behavioral arousal (33), Sleep latency (34), Cognitive functions (35), Spatial working memory (36), Overall behavioral problems in adolescents (33), Enhanced cognitive-motor processes (37), Thermal pain threshold (38), and 'Virtual' spatial navigation task (39). There are also several studies that showed behavioral effects including hyperactive and impaired memory (40), improved cognitive behavior (40), contextual emotional behavior deficit (41), olfactory and/or visual memory deficit in ants (42), food collection behavior of ants (43), decreased motor activity (44), cognitive functions (45), learning and memory deficit (46), hypoactivity (46), improved learning and memory (47), passive avoidance deficit (48), elevated plus maze emotionality test (49), food intake increase (50) and anxiety-related behavior (51). Although a brain uses a great level of oxygen, only a little amount of O2 is converted to ROS. A high level of polyunsaturated fatty acids and wide metabolic rate makes this structure more susceptible to oxidative damages.

Discussion

Effects of Electric and Magnetic Fields on Neural Functions

Long-time exposure to electromagnetic waves increases the standard absorption level and thus extends their damaging effects. Results of some studies have revealed that microwaves emission from mobiles has a vigorous damaging effect on neurons in the cortex, hippocampus and basal ganglia of rats. Moreover, exposure to these waves leads to the increase of two main cell death processes of apoptosis and necrosis in the brain cells of rats. These consequences may be due to the free radicals generated from electromagnetic radiations and result in breaking DNA and cells death. In 1996, Simonian has revealed that nitric oxide and hydroxyl radicals, particularly in nervous cells, may lead to apoptosis (52). These outcomes are consistent with the findings of the study which investigated the effects of 3mT on the brain, cerebellum and spinal cord (53). Electric and magnetic waves can also affect cells genome, cell membrane, intracellular enzyme function, cytoskeleton and the cell nucleus. Under the influence of electromagnetic field, the release of such neurotransmitters as GABA is reduced in Purkinje cells (54). Some results showed the effect of EMFs on calcium level changes in the cell membrane and also increased the activity of ornithine decarboxylase that modifies the expression of DNA (55). Several findings referred to the relationship between exposure duration, the intensity of electromagnetic radiations, and biological effects on neurons. For instance, a research revealed that electromagnetic waves with 60 Hz frequency may increase the number of these cells in respect to exposure duration and dosage of waves. Besides, electromagnetic waves had no effect on DNA synthesis of rat cortical astrocytes (56). Another study also assessed the apoptosis rate of neurons cultured of rats' embryos cortex which were exposed to mobile radiation for 24 hours. The results showed no significant difference in the apoptosis rate between the experimental and control groups (57). Previous findings have reported the breaking of DNA in rats' brain cells, noxious effects on chromosomes in metaphase and chromosomes fracture and chromatin skeleton changes. McNamee indicated that a 60 Hz frequency for 2 hours cannot cause DNA lesion nor apoptosis rate increase in cerebellar granular cells of mouse brain (58). Referring to this case, it can be proposed that these waves increase the formation of hydroxyl free radicals and lead to breaking of DNA bonds. The cells of high iron concentration like proliferating cells and high metabolic activity cells in the brain are the most vulnerable to the wave's adverse effects.

It was also reported that damage to mitochondria of brain cortex in rats under the exposure to a field of 30 Mw/cm^2 leads to mutation in transcription of A-factor and mRNA (59). The permeability of brain blood vessels due to thermal impacts of EMFs waves has been reported. Perhaps, increased vascular permeability is due to the changes in the basement membrane which increase the histamine secretion. There are several studies that show vulnerability of myelinated nerve fibers such as motor neurons to exposure to electromagnetic waves. At the same time, Terada interpreted effects of electromagnetic waves emitted from mobile devices on the human motor cortex. His results suggested that exposure to electromagnetic waves for 30 minutes does not cause changes in the motor cortex neurons or interneuron. Findings of the

proliferating cells revealed that the vulnerable time is during the phase G/S of the cell cycle, when transferrin receptors are expressed and much ion is penetrated. The cells with high metabolic activity synthesize a lot of hydrogen peroxide via the mitochondrial electron transport, hence they become more vulnerable to the electronic and magnetic fields. In addition, the effect of EMF depends on the iron storage ability in the form of ferritin. Therefore, liver cells can be less sensitive to EMF effects because they have many ion inputs, particularly high rates of ferritin. Although the effects of free radicals are very controversial, generally there are four kinds of responses associated with cell attack: Membrane lipids per-oxidation, mitochondrial damages, cross linking creation in proteins and DNA damages. Long-term studies on glioma and acoustic neuroma brain tumors indicate that radial frequencies have carcinogenic impacts (60). In 2011, the study conducted by Nora et al showed an increase in brain glucose metabolism (a symptom for cancer) after exposure to cell phone radiation from nearby antennas (59).

Antioxidants and neural diseases

Antioxidants are broadly used as health supplements to protect body against different age-related diseases. In addition, it has been proposed that the balance between oxidation and antioxidation is critical for preserving the biological system. Low doses of antioxidants are appropriate to biological structures, but high rats may disrupt the necessary equilibrium. Some of brain indexes such as proteins, lipids and nucleic acid oxidation products are the main structures in increasing or decreasing the age-neurodegenerative risks. Oxidative stress is an important key factor in development of neural diseases such as Alzheimer, Parkinson, motor-neurodegeneration diseases, and ALS (61). Thus, preventing free radicals generation or strengthening antioxidants capability can inhibit progression of some neurodegenerative conditions.

It has been reported that antioxidants may fail to protect the blood brain barrier, especially (62). In this regard, most human findings have been collected from vitamin E (alpha tocopherol, αT) treatments or a combination of several vitamin antioxidants. Although certain vitamin E trials in AD have suggested positive effects on quality of life parameters, the findings indicated low or no effectiveness against deterioration conditions of brain functions (63). Long-term treatment via vitamin E studies have suggested an increased rate of hemorrhagic stroke and general mortality and hence increased concerns about severe antioxidant effects at high dosages (64). Some antioxidant supplements have also been used in the treatment of AD. For example, SAM (S-adenosyl methionine) supplementation in ApoE (apolipoprotein E) could not prevent neuro-pathological symptoms of AD. Chan et al showed that apple juice concentrate, as a rich source of SAM, could protect ApoE in AD mice (64). Other dietary supplements including caffeine (65), green tea (66) and red wine have been suggested to inhibit amyloidosis and Aβ production (67) in the cell culture and animal models. Some human clinical trials have been conducted on using vitamin E and various mixtures of vitamin E, selenium, and methionine against ALS. These studies identified no significant impact on primary consequences in the meta-analysis of all antioxidants combined and no remarkable diversity were observed on subsequent measures. Genetic increases of antioxidant enzymes may play a protective role against PD models. For instance, over-expression of Cu, Zn-SOD and glutathione peroxidase (GPx) supported versus paraquat + maneb-induced PD phenotype in mice (68). In 1995, Peyser et al studied a high-dose of α-tocopherol on a cohort of HD patients. They showed that vitamin E had no effect on neurologic or psychiatric signs but the subsequent analyses determined a significant impact of interposition on neurological symptoms in primitive stage patients (69). Consequently, in spite of the few studies available, further research is required to clarify the role of antioxidants on neural functions.

Conclusion

By the studies presented in this review, we can conclude that electric and magnetic waves have a negative impact on the body tissues, especially the CNS. However, this influence depends on various factors such as frequency, wave intensity and duration of exposure. On the other hand, due to complexity in the nervous system, it may be difficult to explain EMFs effects. Antioxidants play an important role against oxidative stress, so they can be used to reduce negative effects of EMFs. However, there are many theories about positive or negative role of antioxidants against EMFs effects on the CNS. In this regard, molecular and cellular examinations are important in expressing the impact of EMFs on neural function. Various types of electromagnetic fields caused to disagreeing ideas among many researchers. Therefore, further studies are needed to identify the probable impacts of herbal and chemical antioxidants on structure and function of the brain neurons.

Ethical Issues

Not applicable.

Conflict of Interests

The authors have no conflict of interest in this study.

Financial Support

None to be declared.

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