ISSN 0001-4338, Izvestiya, Atmospheric and Oceanic Physics, 2012, Vol. 48, No. 8, pp. 832–846. © Pleiades Publishing, Ltd., 2012.
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Interference of the Mechanisms of Influence That Weak Extremely Low-Frequency Electromagnetic Fields Have on the Human Body and Animals

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Abstract—This review is devoted to the problem of interference between the mechanisms of biological action of natural and artificial electromagnetic fields (EMFs) for different levels of the organization of life. We discuss the problem of specific and nonspecific responses of the human body and animals to the action of EMFs on cellular and organismal levels.

Keywords: electromagnetic fields, interference of mechanisms of biological action.

DOI: 10.1134/S0001433812080087

INTRODUCTION

The acceptance of the fact that weak electromagnetic fields (EMFs) are ecologically significant factors influencing many biological processes is one of the advances of science in the 20th century. The natural electromagnetic background, the dynamics of parameters of which are controlled by solar activity and near-earth space weather, as well as by meteorological and hydro-lithosphere processes, constantly influences living creatures [Brutsek, 1980; Miroshnichenko, 1981; Vladimirskii, Temuryants, 2000]. The frequency–amplitude and expositional range of natural EMFs is rather wide; however, the group of extremely low frequencies (ELFs) in the range 10^{-3}–10^{3} Hz is the focus of interest. At the same time, variations in the EMF of the ionosphere waveguide with the central frequency of 8 Hz and different geomagnetic pulsations of magnetic and ionospheric origins are one of the most significant components of the natural EMF of the Earth [Miroshnichenko, 1981; Temuryants et al., 1992; Stepanyuk, 2002, Cherry, 2002, 2003; Aleksandrov, 2005; Kleimenova, 2007]. Environmental "pollution" associated with anthropogenic activity is included to the range of ELFs [Presman, 1968, Grigor'ev, 1997: Tikhonov et al., 1997]. Alongside the main industrial (50–60 Hz) and communication (70–80 Hz) frequencies, noise frequencies of electrotransport (to 10–20 Hz) and resonance frequencies of the ionosphere waveguide driven by electromagnetic waves of anthropogenic origin are of significant ecological importnance [Zabotin, Zhbankov, 1999].

According to the above, it could be assumed that natural variations of electromagnetic background in a wide range of periods are one of the main physical mediators determining the relation between biological phenomena and geo- and cosmophysical processes. However, this idea, which seems simple at first, has been inspiring active discussions for a long time; its experimental proof, according to the literature analysis, is a nontrivial interdisciplinary problem.

There are two basic approaches to managing this question. The first is based on a comparison of series of observations of biological parameters with series of dynamics of cosmo- and geophysical processes. It was this approach that allowed A.L. Chizhevskii and his followers [Chizhevskii , 1995; Vladimirskii, Temuryants, 2000] to reveal the relation between biological, social, and physicochemical processes and solar activity. In this methodological approach, the comparison of spectral analysis results of temporal series of biological and geocosmophysical data is rather informative [Martynyuk, 2005]. A retrospective literature analysis shows the entire spectrum of opinions on this problem: the form negation of the phenomenon of the relation itself to its unconditional acceptance. However, to date most researchers agree with the fact that there is an influence of geophysical processes and processes occurring in the nearest space in the biosphere and, due to that, it is necessary to study not only the nature and mechanisms of such an influence, but also the reasons for its absence mentioned in certain works. It should be mentioned that recently investigations helping us understand the reasons for the bad comparability of the data of different research have been carried out [Kleimenova, Kozyreva, 2008; Zenchenko et al., 2009, 2010].

The second approach is based on an experimental study of the mechanisms of biological activity of EMFs and irradiations in a wide range of frequencies. This approach is more complicated, because it requires understanding between specialists in different fields of scientific activity: physics, biology, ecology, and medicine. Nevertheless, a large array of experimental data persuasively proving the biological activity of weak ELF magnetic fields (MFs) on the order 10^{-4}–10^{-6} T has been already accumulated. There are certain works demonstrating the reliable influence of ELF MFs with induction in the range 10^{-8}–10^{-12} T [Qin et al., 2005], which indicates the extremely high sensitivity of living creatures to this factor. The biological effects of ELF MFs were detected at all organizational levels of life systems. Results from multiple investigations indicate that human behavior [Sidyakin, 1986; Sidyakin et al., 1995; Tokalov, Gutzeit, 2004], the electric activity of neuronal tissue and other electrically active tissues in the human body [Bell et al., 1992, 1994; Breus et al., 2002], the activity of different parts of the neuroendocrine [Temuryants et al., 1992; Garkavi et al., 1998, 1990; Temuryants, Shekhotkin, 1999] and immune [Temuryants, Mikhaylov, 1988; Dumanskii, Nogachevskaya, 1992; Temuryants, Shekhotkin, 1999] systems, the metabolic activity of different organs and tissues [Evtushenko et al., 1978; Chernyshova, 1987; Kolodub, 1989], the activity of certain components of intracellular signalization [Goodman, Henderson, 1988; Graviso et al., 1995; Lyburdy, Eckert, 1995], and the synthesis of proteins and nucleic acids [Goodman et al., 1983; Goodman, Henderson, 1986; Blank, Goodman, 2001; Lin et al., 2001] in cells change under the effect of ELF MFs. Electromagnetic shielding also causes notable changes in the activity of biological processes [Temuryants et al., 2008]. There are also theoretical and experimental data on the influence of ELF MFs on structural and functional characteristics of proteins and nucleic acids [Fesenko et al., 1997; Novikov et al., 1999]. However, in spite of plenty of evidence of the biological activity of ELF MFs, researches notice that results received at different times by different scientists are not easily comparable with each other and are often contradictory, which significantly complicates understanding both the primary and system mechanisms of ELF MF action [Bingi, 2002]. At the same time, the question about the "interference" of possible primary mechanisms of the influence of the given physical factor and their integration on cellular and organism levels is extremely rarely raised in literature.

The analysis of extensive literature on electromagnetic biology and the results of personal studies indicate that the effects of ELF MFs similar in characteristics to EMFs of natural and anthropogenic origins are observed at all levels of organization of life systems. At the same time, ELF MFs, as the factor penetrating everything, simultaneously influence cells and tissues of the body; for that reason, at different levels of organization, split-level effects are synchronously realized which, on a systematic level, appear as nonspecific adaptation reactions. Such nonspecific reactions are observed on cellular and organism levels.

Another important feature of the influence of EMFs on life systems should also be mentioned. In most experimental studies, the response of a cell or a multicellular organism is registered within the limits of the physiologic reaction norm, i.e., within such limits in which common reactions to other nondisturbing stimuli take place. Only under the effect of relatively strong and lasting exposure to electromagnetic factors are specific pathologic alterations registered. Due to that, researchers often are interested in the question of whether the influence of EMFs on living organisms is specific. If yes, then in what form and at what level is this specificity realized? The answer to this question is impossible without understanding the mechanism of influence of EMFs on molecular, cellular, and organism levels.

Primary Mechanisms of the ELF MF Effect

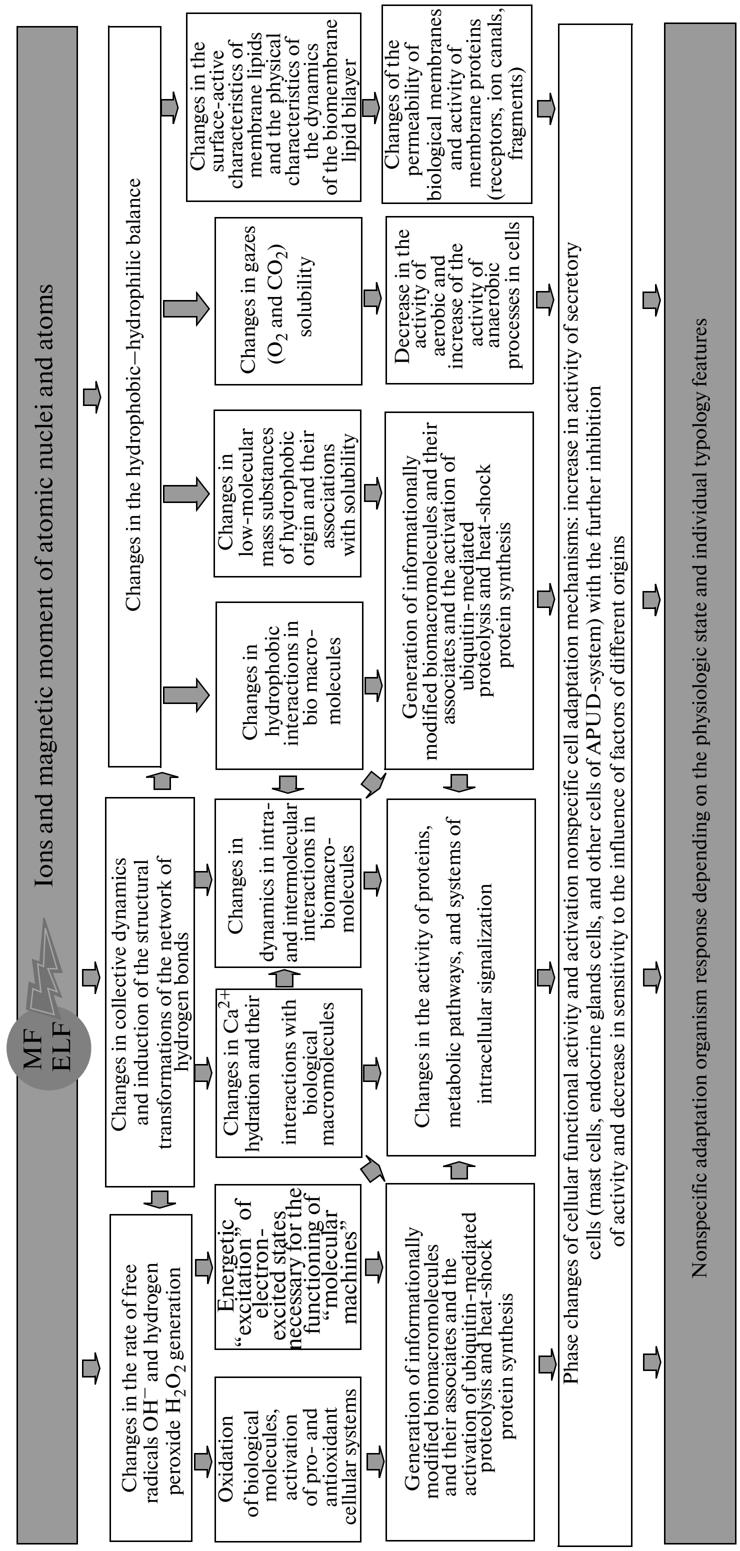
At the current stage of development of electromagnetic biology, there is a series of theoretical conceptions of the primary mechanisms of the biological effect of weak ELF MFs [Bingi, 2002]. However, the examination of ELF MFs on the cellular level already requires taking into consideration the "interference" of different mechanisms on the molecular level, which can be simultaneously achieved in the cell. A literature analysis and the results of personal studies by the authors allowed integrating current conceptions on mechanisms of a weak ELF MF influence on molecular and cellular levels in the form of the scheme in the figure.

Among currently suggested mechanisms of ELF MFs on the primary molecular level, the so-called resonance and water mechanisms are of the greatest interest.

Ion-Resonance Mechanisms

The essence of "ion-resonance" hypotheses is the fact that biologically significant ions are the "targets" of ELF MF action. Hypotheses are based on experimental results. It was established that, for several models of biological processes, maximal magnetobiological effects are observed at frequencies actually equal to the frequencies of cyclotron resonance in the geomagnetic field of such biologically important ions as Ca^{2+}, Mg^{2+}, K^{+}, Na^{+} [Lednev et al., 1996; Belova et al., 2010]. Certain theoretical interpretations of how ELF MFs influence the counteractions between ions and proteins were proposed and attempts were made to prove them experimentally [Blackman et al., 1994; 1995; Lednev at al., 1996].

Conclusions to the discussion of this question show that the proposed theoretical explanations from the classic physical point of view are not sufficiently correct and the experimentally observed magnetobiological effects may be explained on the basis of quantum interference [Bingi, 2002, 2004] and different variants



Interference of the main mechanisms of influence of ELF MFs on physicochemical, molecular, and cellular levels. Descriptions in the text.

of spin conversion [Drozdov et al., 2010]. At the same time, the community of known resonance phenomena and "ion resonances" typical for the magnetic moment of atomic nuclei and electron orbits are clearly seen, which obviously indicates the common quantum origin of the observed phenomena [Zakharov, 2010]. The consideration of this problem from a quantum physics point of view allows us not only to newly see the physical essence of "ion resonance" and other events but it also opens up more extensive prospects for theoretically explaining the magnetobiological effects [Bingi, 2002].

The theoretical conceptions mentioned above do not explain the entire variability of known magnetobiological effects. This is associated with the fact that ions and other components of life systems which can be the targets of ELF MFs "work" in particular according to the characteristics of the condensed medium (in water).

The Influence of ELF MFs on Physicochemical Characteristics of Water, Aqueous Solutions, and Colloid Systems

The fact that the water phase, the quasicrystal structure of which is actually in the metastable state and constantly changes due to spontaneous free-radical processes and spontaneous transformations of hydrogen bonds, is the primary acceptor of weak EMFs is the essence of the water hypotheses [Bingi, 1998; Betskii et al., 2003; Akopyan, Airapetyan, 2005]. This metastable dynamical state is the key factor of the sensitivity of the water phase to weak ELF MFs. At the same time, factors structuring water, i.e., promoting the formation of cluster and clathrate cavities, enhance the sensitivity of the water phase to electromagnetic exposures [Colic, Morse, 1998]. The exposure of factors of different origins, including ELF MFs, changes the dynamics of structural transformations [Kalinina et al., 2003; Kholmogorov et al., 2003; Chernikov, 1990a, 1990b, 2003], which leads to changes in the structure of water clusters and larger water constructions of different origins [Ponomarev, Fesenko, 2000; Lobyshev et al., 2003; Smirnov et al., 2004; Martynyuk, Nizhelskaya, 2009]. Taking into consideration the fact that water is a certain biological matrix determining the organization of the surface of biomolecules and their spatial structure in general [Bullienkov, 1998; Lobyshev et al., 2003]and is also one of the factors determining the micro- and macroscale dynamics of molecular constructions [Kyaiveryainen, 1980, 1989], MF-induced changes of water phase dynamics should lead to corresponding changes in the intramolecular segments of protein-molecule dynamics [Il'ina et al., 1979; Kyaiveryainen, 1989; Slesarev, Shabrov, 2006] and, as a consequence, to the changes of structural and functional protein characteristics.

One more biologically significant water-mediated canal of the influence of ELF MFs on life systems is considered in literature: the influence of EMFs on the stability of Ca^{2+} ions in water systems. These ions are one of the universal intracellular messengers in different pathways of cell signalization and regulate a wide range of intracellular processes. The increase in concentration of free Ca^{2+} ions in a cell switches it, as a rule, into an active functional state. It is well known that Ca^{2+} ions are ions which decrease the water structural temperature; i.e., Ca^{2+} ions promote the stabilization of hydrogen bonds, being structural stabilizers of water [Privalov, 1968; Kislovskii, 1989, 2005]. Taking into consideration the fact that structuring substances increase the sensitivity of water systems to the effect of weak electromagnetic factors [Colic, Morse, 1998] as well as the extremely significant biological function of calcium ions as "information mediators" in the system of cell regulation, it becomes clear how the biological effects of EMFs are often directly associated with the condition of these ions in the cell.

It is quite important that in many experimental trials the resonance response of bio systems on ELF MF action was shown; the response is actually achieved on the frequencies of the Ca^{2+} ions cyclotron resonance. This proves the fact that physicochemical and molecular-biological processes determining the concentration of free Ca^{2+} ions and probably the stability of its hydrate cover are one of the targets of action of ELF MFs in biological systems. Due to that, we cannot exclude that the increased biological activity of MFs on "cyclotron" frequencies is associated not with the influence of a given factor on the condition of Ca^{2+} ions in protein binding sites, but with the effect on the stability of Ca^{2+} hydrate covers and clathrates stabilized by the hexaaquacomplexes of these ions and thus on the ration of free forms of the given ion and those bound with biomolecules [Kislovskii, 1989, 2005].

On the basis of conceptions developed by L.D. Kislovskii [Kislovskii, 1989, 2005], it could be assumed that the dynamic structure of water in the cell in the functionally inactive state does not allow ions to form a stable hydrate cover and, due to that, the equilibrium is shifted to the side of association of Ca^{2+} ions with biomacromolecules. However, if ELF MF exposure induces structural transformations to break the structural "ground" of the functionally inactive state, then Ca^{2+} ions are hydrated, proceed to the free state, and promote the formation of new structural functionally active "ground" in the dynamic structure of water. At the same time, if ELF MFs affect a biologic object in the functionally active state, which is imprinted in the dynamic state of water, then the reverse process may be possible; i.e., Ca^{2+} ions will lose their hydrate cover and transform to the bound state, thus moving the cell into the inactive (or other) functional state. Thus, the given hypothesis to a certain extent allows interpreting the phenomena of activating and normalizing (anti-stress) the effect of ELF MF [Garkavi et al., 1990; 1998; Temuryants, 1992; Temuryants et al., 1992; Temuryants, Shekhotkin, 1999], which could not be explained on the basis of the conception of ion resonances. The works of Lednev et al. [Belova et al., 2003] show the possibility of influencing MFs actually adapted to "ion parametric resonance" in the geomagnetic field on calcium carbonate aqueous solutions, which, in our opinion, confirms the correctness of the "water" hypotheses.

In scheme proposed by us (figure) it is shown that MF-induced changes in the dynamical structure of water lead to changes in the hydrophobic–hydrophilic balance in water systems, which is realized in changes in the solubility of nonpolar substances (as a rule, decreasing) in water and their counteractions with biomacromolecules (as a rule, enhancing) [Martynyuk, Shadrina, 1999; Martynyuk et al., 2003; Martynyuk, Tseysler, 2006]. The shift of the hydrophobic–hydrophilic balance influences changes of hydrophobic counteractions in macromolecular structures, which is probably one of the main reasons for the dynamic conformation transformations in proteins registered by the authors [Martynyuk et al., 2004; Martynyuk et al., 2004], as well as by other researchers [Serpersu, Tsong, 1983: Fesenko et al., 1997; Shvetsov et al., 1998; Antropov, Maksimov, 1999; Novikov et al., 1999]. At the same time in experimental models in which the load of macromolecules by low-molecular mass hydrophobic structures is observed, the effects of ELF MFs influencing structural characteristics are significantly higher [Martynyuk, Tseysler, 2006]. Considering the fact that certain substances acting in life systems as signal and regulatory (steroid enzymes, intracellular messenger diacylglycerol, etc.) mechanisms have pronounced hydrophobic characteristics, different functional changes may be expected both from the side of individual cells and from the side of entire organs and functional systems of a multicellular organism.

It is well known that gases, including oxygen, dissolve in water by the hydrophobic mechanism [Cantor, Schimmel, 1984]. At the same time, the gases are presented either in a truly dissolved state or in the form of nanobubbles and their fractal organized aggregates [Bunkin et al., 2009]. Unsurprisingly, the transformations of the dynamic structure of water induced by EMFs lead to a decrease in air solubility and a decrease in oxygen and carbon dioxide concentration in cells and the intracellular medium [Stashkov, Gorokhov, 1998; Emets, 2000]: the activation of anaerobic processes is a cellular response to such changes. Probably, for that reason, many researchers mentioned an increase in the activity of glycolytic reactions and an increase in lactic acid production in different tissues [Evtushenko et al., 1970, 1978; Kolodub, 1989]. Simultaneously, a decrease in carbon dioxide concentration also can lead to undesirable effects, especially if the question is about acid-base balance maintenance in blood and processes of the complementary regulation of oxygen and carbon dioxide transport in blood. The fact that the gas phase in the water medium plays the initial part in the structural organization and function of biological macromolecules [Pivovarenko, Martynyuk, 2009; Shatalov, 2009; Doshi et al., 2010] should be emphasized.

Changes in the hydrophobic–hydrophilic balance induced by ELF MF action also influence the manifestation of the surface-active characteristics of phospholipids and other substances of natural origin [Panova et al., 1998; Martynyuk, Panov, 2001; Martynyuk, Panov, 2004]. Such changes probably cause alterations in membrane permeability [D'Inzeo et al., 1993; Ramundo-Orlando et al., 1995] and their hydrophilia and hydrophobicity [Fesenko, Gluvstein, 1995]. Form the other side, upon such changes in physical and chemical characteristics of the membrane, the Ca^{2+}-independent stimulation of spontaneous secretion of the content of cytoplasmic granules due to their confluence with the plasma membrane may be expected. At the same time, increased membrane permeability for Ca^{2+} ions and/or their transmission to a free state will additionally stimulate Ca^{2+}-dependent secretion regulation pathways. Such a combined (dependent and independent of Ca^{2+} ions) mechanism of ELF MF action is probably dominating in secretory cells [Martynyuk, Abu Khada, 2001, 2003; Martynyuk et al., 2001a], which secrete different biologically active substances and participate in the formation of a generalized response on the organism level. The group of these cells in human and animal bodies is considered a separate functional system of diffusely dispersed cellular elements: the amine precursor uptake and decarboxilation (APUD) system [Luk'yanchikov, 2005]. It plays the initial role in mechanisms of the effect of ELF MFs on regional (tissue) and organismal levels.

The Influence of ELF MFs on the Generation of Active Oxygen Forms

According to the literature data, there is one more canal of ELF MF influence on biological processes mediated through the structural transformations of water. It is associated with the fact that these structural transformations in the regions of cluster interactions are accompanied with the rupture of covalent bonds in a water molecule and the generation of hydrogen atoms and $OH^{\bullet}$-radicals [Voeikov, 2006]. It is considered that the probability of the indirect influence of weak (less than 100 μT) ELF MFs on the recombination of free radicals is significantly low and, for that reason, the biological effects of a given factor will be defined chiefly by the rate of free-radical generation. However, recent investigations have shown a principal opportunity of ELF MFs to also influence the recombination of radical pairs, and this influence is nonmonotonous and depends on the MF frequency and amplitude [Shigaev et al., 2003].

The modulation of free-radical generation in water and their recombination under the influence of ELF MFs, which have been shown even in the works of J. Piccardi [Piccardi, 1967], must induce alterations in the lipid peroxidation of biological molecules and, as a consequence, the activity of anti- and prooxidative systems in the cell. It is quite possible that experimentally observed changes in the state of the thioldisulfide metabolism and lipid peroxidation processes [Martynyuk V.S., Martynyuk S.B., 2001b, Martynyuk et al., 2001; Martynyuk, Kuchina, 2004] are associated to a certain extent with the named mechanism of ELF MF influence. Experimental data on the MF-induced acceleration of protein hydrolysis in aqueous solutions [Shvetsov et al., 1998; Novikov et al., 1997, 2000; Novikov, 2005] may be explained by the MF-induced increase of free-radical generation in water. Simultaneously, an increase in DNA ruptures upon the exposition of cells in ELF MFs [Testa et al., 2004] also may be explained by the activation of free-radical processes.

Recently, certain researchers [Blank, Goodman, 1995; Voeikov, 2006] have considered the spontaneous generation of active oxygen forms in water natural and necessary processes providing the energy "excitation" of the metastable water state. This energetic excitation is conducted through the influence on water and water systems by different factors, including ELF MFs. At the same time, it is emphasized that the energy of electron and vibron excitation in water generated in recombination reactions of radical pairs is used by "molecular machines" for the performance of their working plans. In relation to that, it is supposed that ELF MFs influencing free-radical generation in water indirectly affect the intramolecular dynamics of molecular machines—proteins, thus increasing or decreasing their functional activity. It is logical to assume that the nature and orientation of such changes should depend first and foremost on the nature of protein and its initial functional state.

Generation of Modified Protein Forms

MF-induced changes of hydrophobic interactions in biomacromolecules and the binding of nonpolar molecules with biopolymers and membranes, changes in lipid bilayer characteristics, and free-radical generation lead to the appearance of structurally modified protein forms (figure). At the same time, the probability that MF-induced structural modifications will occur significantly increases under conditions of the functional load of protein [Martynyuk, Tseysler, 2006], at which they experience natural conformation transformations [Kyaiveryainen, 1980, 1989].

Such influence of ELF MF leads not only to the formation of conformationally modified macromolecules, but also to that of protein aggregates, which on the one hand activates ubiquitin-mediated proteolysis system activation and, on the other, induces heat-shock protein synthesis [Blank, Goodman, 1995; Goodman et al., 1995; Tokalov, Gutzeit, 2004]; these proteins, as is well known, have protective function via their association with biomacromolecules and are one of the main components of nonspecific cellular adaptation mechanisms [Hinault, Goloubinoff, 2007]. This explains the increased cell sensitivity to stress factors and ionizing radiation effects after their preliminary exposition in a MF [Kopylov, Troitskii, 1982; Kudryashov et al., 2006] and the increase in the harmful influence of factors when they act simultaneously with ELF MFs [Kopylov, Troitskii, 1982; Tomashevskaya et al., 1999; Koyama S. et al., 2005; Kudryashov et al., 2006].

Thus, an analysis of the literature and the results of personal experiments make it possible to conclude that water hypotheses are the most universal for explaining and understanding the mechanisms of specific and nonspecific ELF MF effects. However, it should be kept in mind that, in the hierarchy of organization levels of biological systems, these are second-level hypotheses, i.e., physicochemical. Water hypotheses can explain the remote influence of EMFs and the biological activity of magnetized solutions [Il'ina et al., 1979; Huib, Bakker, 1999; Bingi, 203; Slesarev, Shabrov, 2006]; for that reason, the given research field can be considered one of the most interesting and prospective in modern electromagnetic biology.

Biological Mechanisms of ELF MF Action

In the lower part of the scheme in figure it is shown that the abovementioned complex of MF-induced changes in different processes and their interference lead to a generalized cell reaction, depending either on the functional specialization of the cells or on their functional state (rest, activity, or stress), which determines whether the functional activation of the cell or its activity suppression will occur upon the simultaneous activation of the nonspecific cellular adaptation reaction complex.

Literature data indicate that the expression and direction of the mentioned MF effects depend on the frequency of ELF MFs; thus "frequency effects" themselves depend on the amplitude of both variable and constant MF components, on the background of which the exposure of variable component is conducted. This on the one hand significantly extends the spectrum of possible biologic effects and on the other creates great problems for the reproducibility of experimental results obtained by different research groups.

Thus, understanding ELF MF specificity is complicated by the fact that, in the cell, all listed mechanisms are achieved simultaneously; which factor makes a greater contribution to generalized reaction depends on cell functional specialization, its initial physiological state, and frequency–amplitude and magnetic-field exposure expositional characteristics. Due to that, there is great number of ELF MF effects received on different molecular and cellular models, which cannot be easily compared or theoretically interpreted, resulting in justifiable agreement from fundamental scientists.

In spite of the presence of multicanal ELF MF exposure on the molecular and physicochemical level, the generalized specification of the reaction of the cell to the action of the same factor depends on structural–functional cell specialization. The group of organismal cell elements demonstrating higher sensitivity and reactivity to ELF MF action can be highlighted [Temuryants, Shekhotkin, 1999; Martynyuk, Abu Khada, 2001, 2003]. Practically all of them are cells of the APUD system.

APUD-System Cells as ELF MF Sensors

As is well known, the APUD system, along with nervous and endocrine systems, is a specific integrative system of organismal regulations which consists of special cells: apudocytes located everywhere in tissues and having specific ultrastructural and cytochemical characteristics. The presence of cytoplasmic (associated with the cell membrane) microgranules filled with biologically active substances is an ultrastructural feature of apudocytes. The opportunity to consume and split monoamines, or, more exactly, 5-hydroxitryptophane and L-dihydroxiphenylalanine (from which biogenic amines and peptide enzymes are synthetized), is the cytochemical specification of these cells. It is these cytochemical characteristics that are reflected in the abbreviation APUD. In the Russian-language literature, this system was called the diffuse neuroimmuneendocrine system.

The APUD system combines the nervous, endocrine, and immune systems into a united complex with doubling and partially interchangeable structures and functions. Its physiological role is to regulate all biological processes on all levels (from subcellular to system) [Luk'yanchikov, 2005]. The APUD system consists of nearly 60 cell types found in CNS (hypothalamus and cerebellum), endocrine glands (hypophysis, epiphysis, thyroid gland, pancreas insulae, adrenal glands, and ovaries), thymus and lymphatic nodes, gastrointestinal tract, lungs, kidneys, urinary tracts, placenta, and connective tissue. Mast cells, thyrocytes, endocrine cells of the gastrointestinal tract, adrenal chromaffin cells, hypothalamus neurosecretory cells, epiphysis pinealocytes, parathyrocytes of parathyroid glands, and leukocyte granulocytes, as well as endocrine cells of adenohypophysis, placenta, pancreas, respiratory tract, kidneys, skin and other organs and tissues, are all the cells of APUD-system.

One feature of these cells is that they are located near blood vessels among epithelium and connecting-tissue cells. Apudocytes synthesize the wide range of mediators and tissue hormones (histamine, serotonin, melatonin, adrenaline, noradrenalin, and DOPA), including peptide (somatotropin, cytokines, ACTH, ADH, endorphins, enkephalins, tumor necrosis factor, etc.) and steroid origins (testosterone, progesterone, and estrogens). Under normal conditions, the apudocyte secretion of given substances is conducted under the effect of external stimuli.

Our investigations have shown high sensitivity of mast cells to EMF action both in in vitro and in vivo conditions [Martynyuk, Abu Khada, 2001, 2003]. At the same time, there are data on EMF-induced changes in the functional activity of pinealocytes [Lerchl et al., 1991]; adrenal medulla cells [Goodman, Henderson, 1988]; granular leukocytes [Nordenson et al., 1984], and cells of the hypothalamus [Bogolyubov et al., 1992], hypophysis [Moroz, 1984], and thyroid glands [Vorontsova et al., 1999].

Thus, under the action of ELF MFs on the entire organism, each tissue and organ reacts according to the cell representation of the APUD system in it and the character of its cell-element distribution. For example, in connective tissue in the intercellular space and also under in vitro conditions, mast-cell activity increases [Martynyuk, Abu Khada, 2003]. Taking into consideration the wide range of biological activity of substances excreted by mast cells, the initiation of a reaction cascade eventually leading to changes in electrolyte, energetic, trophic and gaze-transport balance occurs. Such a progression of events should in the first instance lead to an increase in the functional load of cardiovascular and central nervous systems. Probably, due to that, during geomagnetic disturbances and storms caused by changes in space weather and also during the periods of rapid changes in atmosphere dynamics accompanied with electromagnetic spikes [Aleksandrov et al., 2005], the risk of hypertonic crises, insults, and heart disorders rises [Ptitsyna et al., 1998; Breus et al., 2002; At'kov et al., 2006]. The development of the mentioned complex of tissue homeostasis in CNS as a response to changes in the electromagnetic background leads to attention reduction and, as consequence, an increase in the risk of plane crashes and car accidents [Sidyakin, 1986; Zenchenko et al., 2006].

In an immune system, ELF MF actions directly activate polymorphonuclear leukocytes [Temuryants, Mikhaylov, 1988], which is eventually reflected in nonspecific resistance characteristics [Temuryants, Mikhaylov, 1988; Temuryants, 1992; Temuryants, Shekhotkin, 1999]. The MF-induced activation of adrenal medulla cells increases the catecholamine level in blood [Craviso et al., 1995]. The magnetic sensitivity of gastrointestinal apudocytes is not well studied; however, it may be logically assumed that these cells react stereotypically to ELF MF action. Thus, MF-induced functional changes in different organs and tissues are a signal to CNS about homeostasis changes; as a response to that, the hypothalamus–hypophysis–adrenal system is activated in the organism and a complicated adaptation reaction cascade directed toward restricting or modifying the functional activity of certain functional systems and enhancing the activity of others is initiated. Due to that, at the organismal level there is now evidence for expecting specific reactions to ELF MF action.

The nature of developed nonspecific adaptation changes depends either on ELF MF parameters (frequency, amplitude, and exposition) or on the initial physiologic state [Garkavi et al., 1990; 1998; Temuryants, 1992; Temuryants et al., 1992a, 1992b] and individual typology features [Temuryants, Grabovskaya, 1992; Temuryants et al., 1995; Temuryants, Shekhotkin, 1999] of human and animal bodies.

The human body probably has a different reaction to geomagnetic disturbances in summer and winter months for this reason [Kleimenova, Kozyreva, 2008], because in these months the adaptation abilities of an organism are significantly different. At the same time, short-lasting and short-period ELF MF exposure cause nonspecific adaptation reactions ("activation" and "training") on the organismal level [Garkavi et al., 1989, 1990; Temuryants, 1992], whereas the strong and lasting exposure of a given factor in combination with other exposures lead to the development of functional changes in the Selye stress-reaction type [Izmerov at al., 1996].

Induction Mechanisms and Stochastic Resonance in Life Systems

The abovementioned cascade of biological mechanisms of the ELF MF effect does not exclude other pathways for the influence of the given factor on multicellular organisms. Thus, on an organismal level, induction mechanisms are possible. The complex system of electrically conducting circuits in human and animal organisms is the physical base for their occurrence; in these circuits, according to Faraday's law, a variable MF generates an electric field, which in electrically conducting circuits leads to the appearance of an electromotive force. The possibility of such phenomenon is described in details in the work [Ptitsyna et al., 1998]. Nervous, cardiovascular, and lymphatic systems are obvious examples of such three-dimensional systems of electrically conducting circuits. Upon variations in the magnetic induction flow in such circuits, variable electromotive forces occur in the range of ELFs, which are accepted by neurons. According to calculations, the value of induced electromotive forces in a 1-V/m electrical field in the electrically conducting circuit of cell sizes is 10^{-4} V [Bingi, 2002]. This is very a small value, so signal enhancement may be performed by increasing the number of turns in the circuit or increasing its sizes. Such enhancement in humans and animals is possible if we take in consideration the fact that linear sizes of neuronal, lymphatic, and vascular electrically conducting circuits connected serially and parallel could be from several millimeters or centimeters do several meters. In this case the values of the induced electromotive force can reach tens of millivolts, which is enough for the threshold depolarization of neuronal membrane and a spike in potential development.

The additional enhancement of extreme weak electromotive forces induced by natural and anthropogenic ELF MFs may be conducted through the mechanism of stochastic resonance. The phenomenon of stochastic resonance is the redistribution of the metastable system dynamic variable force spectrum under the influence of a weakly determined force against the background of additive noise. It was shown that the given mechanism may be achieved on the level of neuronal networks to enhance weak signals [Kruglikov, Dertinger, 1994] or in ion canals located in bio membranes [Bezrukov, Vodyanoj, 1997; Galvanovskis, Sandbiom, 1997]. The occurrence of a weak electric signal, e.g., as a result of induction mechanisms overlapping occasional variations of certain parameters, for example, subliminal variations of membrane potential, is the essence of the given mechanism. As a result of such overlapping, the probability of membrane-potential fluctuations of the threshold level and spike-potential generation increases. The stronger the periodic signal overlapping the threshold fluctuations is, the higher the probability of a spike potential is. It is significant that the growth in sensitivity of such a system to weak periodic exposure may be also reached by an increase in its internal noise.

It should be mentioned that there is one more reliable mechanism for enhancing weak electric subliminal fluctuations of membrane potential in the nervous system. This is the well-known mechanism of the spatial–temporal summation of subliminal potentials. The complicated three-dimensional system of organismal "electrically conducting" circuits can act as a highly sensitive ELF MF sensor with high amplification gain. It is possible that the "magnet compass" of birds and animals that helps them orientate in space functions on this induction–stochastic–resonance principle [Diego-Rasilla et al., 2005]. Then the reasons why birds get disoriented during spikes in geomagnetic activity become clear [Shreiber, Rossi, 1979]. Because geomagnetic impulses are characterized by different polarities and different spins of polarization planes, the resulting geomagnetic vector, the location of which is monitored by the magnet navigation system of the bird's brain, is constantly fluctuating; as a result, the trajectory of bird flight becomes more chaotic and the flight takes more time.

The mechanism of stochastic resonance may be successfully applied to explain individual typology features of organismal reactions to the ELF MF effect. The noise that is always present in physical and biological systems (e.g., subliminal fluctuations of membrane potential), which is one of the factors increasing the sensitivity of the "magnetic biodetector," is the most significant feature of the given mechanism. In biological systems the noise level may be regulated parametrically (e.g., the regulation of the spontaneous excretion of neuromediator quants in synaptic gap or activity of monoaminooxidases regulating neuromediator concentration in synaptic gap). This allows the organism to change its ELF MF sensitivity range, which is significant for its adaptation to environmental changes. However, the activity of molecular and cellular systems performing parametric noise regulation is also changing under the influence of ELF MFs. In this case, interference of a mechanism with a different origin that takes place on different organization levels may be expected and, as a result, the additional enhancement or attenuation of an incoming signal or a compensation for effects occurs. Respectively, expressed sensitivity and reactivity of the organism to ELF MF action or weak reaction or the absence of any effect may be expected.

In should be mentioned that the experimental data demonstrative the dependence of organismal reactions to ELF MF action on its individual typology features [Temuryants et al., 1995; Martynyuk V.S., Martynyuk S.B., 2001; Martynyuk et al., 2001b]. It was shown that animals with low activity in an "open field" react to ELF MF more actively. One of the reasons for such sensitivity is probably associated with the higher excitability of CNS compartments responsible for the generation of negative emotions of fear and anxiety. Such features of organization of processes in CNS at the first instance determine the character of neuroendocrine regulation in the organism. It may be assumed that in underactive (in the "open field") neuronal brain structures responsible for the mentioned emotions, the "noise level" is higher, which yields the high sensitivity of the given CNS compartments to the effect of different factors bringing additional signals, including ELF MFs. The corresponding hormonal background typical for a given group of animals probably increased the base level of stress hormones in blood [Koplik, 1995a,1995b] and additionally promotes the maintenance of increased excitability of different compartments of their brain and, as a consequence, high sensitivity to ELF MF action.

It should be mentioned that, for the system mechanisms of ELF MF action under consideration, there are probably no principal differences in what type of signal is brought: periodic or noiselike. A comparative analysis of literature data and personal investigations into the influence of impulse ELF MFs with a frequency of 8 Hz and an MF with a complicated spectrum has shown that, on a system level, a similar stereotypical nonspecific reaction develops; its occurrence depends to a greater degree on individual typical features of the animals than on the MF-frequency characteristics [Martynyuk et al., 2001a, 2001b]. Nevertheless, it is still too early to provide the final answer to this question. This problem is the focus of great theoretical and practical interest and requires further study.

Synchronizing Effect of ELF MFs

Unfortunately, modern geomagnetic indexes do not reflect the spectral compounds of geomagnetic variations, though this question is discussed and attempts are even made to solve it [Kleimenova, Kozyreva, 2008], because, in spite of the stereotype of response reactions on the organismal level, the spectral compound of the acting ELF MFs can be significant for the structure of biological rhythms. In earlier investigations we have found the frequency dependence of changes in the ultradian rhythm of metabolic characteristics [Martynyuk, 1992a, 1992b]. In these investigations we have also found the effects of synchronization of metabolic processes in the utradian biorhythm range. Further, we have conducted a cycle of works with the aim of confirming the synchronizing influence of ELF MFs similar in frequency characteristics with natural variations in the range of the ionosphere wave guide to biorhythms at the infradian range [Grigor'ev et al., 2004; Temuryants et al., 2004, 2006]. The results of investigations indicate that the synchronizing influence of ELF MFs is also observed in the infradian range [Martynyuk, Temuryants, 2009]. At the same time, according to the results of investigations, the phenomenon of imprinting the rhythmic organization of geoheliophysical processes in the structure of organismal biorhythms was established; it can be explained by the influence of ELF MFs of natural origin [Grigor'ev, Martynyuk, 2003].

CONCLUSIONS

Thus, the hypothesis considering stable variations in the natural EMF to be a sensor of biorhythm time [Temuryants et al., 1992a, Vladimirskii, Temuryants, 2000] has been newly experimentally proven. Nevertheless, the problem of the influence of MFs on biorhythms is far from being completely solved. Particularly, questions on the dependency of biorhythmic parameters on MF frequency and the amplitude, exposition, and recurrence of the exposure remain open. On the basis of current conceptions of the processes of synchronization in physical and biological systems [Pikovskii et al., 2004], the presence of more complicated frequency–amplitude modes of synchronization of different biological processes in a wide range of periods may be expected [Martynyuk et al., 2004]. At the same time, it is important to thoroughly study the effects of interference of MFs on different levels of organization of biological rhythms.

Taking into consideration the complexity of the mechanisms of biological influence from EMFs on life systems at different organization levels, it becomes clear that researchers searching for correlations of processes in human and animal organisms with geo and cosmophysical processes have very difficult tasks. Firstly, the functional state of the organism (norm, activation, stress, and pathology); its constitutional features; and features of the intadaily, daily, and multidaily temporal organization of the studied biological processes must be taken into consideration. Secondly, generally accepted geomagnetic indexes are not always effective in studying correlations between cosmophysical and biological processes, so the development of new special electromagnetic indexes characterizing the electromagnetic situation in the range of frequencies confirming to, e.g., ion and magnet resonances important for life systems is an important task. Such ranges are ranges 1–7 (ion cyclotron forms of low-molecular mass organic substances: amino acids, biogenic amines, etc.), ranges 7–20 (ion cyclotron resonances of Cu^{2+}, Cu^{+}, Zn^{2+}, Cl^{-}, K^{+}, OH^{-}), 20–40 (ion cyclotron resonances of Na^{+}, Ca^{2+}, Fe^{2+}, Fe^{3+}), and 600–800 Hz (ion cyclotron resonance of H^{+}). Attention should probably also be focused on the ranges of magnetic resonance of protons in the geomagnetic field 1.8–2.2 kHz and electron paramagnetic resonance 1–2 mHZ for the active oxygen forms $O_2^{-\bullet}$, $OH^{\bullet}$ and organic radicals. Currently there are no such indexes; however, there have been some early attempts to establish them [Kleimenova, Kozyreva, 2008]. At the same time, it is clear that such new indexes should be regional, and that requires the creation of a new network of electromagnetic monitoring. The system of regional monitoring of Schumann resonances developed by researches from Tomsk with open data access (http://sosrff.tsu.ru/) may be used as the basis.

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