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Extremely Low Frequency Electromagnetic Fields as Effectors of Cellular Responses In Vitro: Possible Immune Cell Activation

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Abstract There is presently an intense discussion if electromagnetic field (EMF) exposure has consequences for human health. This include exposure to structures and appliances that emit in the extremely low frequency (ELF) range of the electromagnetic spectrum, as well as emission coming from communication devices using the radiofrequency part of the spectrum. Biological effects of such exposures have been noted frequently, although the implication for specific health effects is not that clear. The basic interaction mechanism(s) between such fields and living matter is unknown. Numerous hypotheses have been suggested, although none is convincingly supported by experimental data. Various cellular components, processes, and systems can be affected by EMF exposure. Since it is unlikely that EMF can induce DNA damage directly, most studies have examined EMF effects on the cell membrane level, general and specific gene expression, and signal transduction pathways. In addition, a large number of studies have been performed regarding cell proliferation, cell cycle regulation, cell differentiation, metabolism, and various physiological characteristics of cells. Although 50/60 Hz EMF do not directly lead to genotoxic effects, it is possible that certain cellular processes altered by exposure to EMF indirectly affect the structure of DNA causing strand breaks and other chromosomal aberrations. The aim of this article is to present a hypothesis of a possible initial cellular event affected by exposure to ELF EMF, an event which is compatible with the multitude of effects observed after exposure. Based on an extensive literature review, we suggest that ELF EMF exposure is able to perform such activation by means of increasing levels of free radicals. Such a general activation is compatible with the diverse nature of observed effects. Free radicals are intermediates in natural processes like mitochondrial metabolism and are also a key feature of phagocytosis. Free radical release is inducible by ionizing radiation or phorbol ester treatment, both leading to genomic instability. EMF might be a stimulus to induce an ''activated state'' of the cell such as phagocytosis, which then enhances the release of free radicals, in turn leading to genotoxic events. We envisage that EMF exposure can cause both acute and chronic effects that are mediated by increased free radical levels: (1) Direct activation of, for example macrophages (or other cells) by short-term exposure to EMF leads to phagocytosis (or other cell specific responses) and consequently, free radical production. This pathway may be utilized to positively influence certain aspects of the immune response, and could be useful for specific therapeutic applications. (2) EMF-induced macrophage (cell) activation includes direct stimulation of free radical production. (3) An increase in the lifetime of free radicals by EMF leads to persistently elevated free radical concentrations. In general, reactions in which radicals are involved become more frequent, increasing the possibility of DNA damage. (4) Long-term EMF exposure leads to a chronically increased level of free radicals, subsequently causing an inhibition of the effects of the pineal gland hormone melatonin. Taken together, these EMF induced reactions could lead to a higher incidence of DNA damage and therefore, to an increased risk of tumour development. While the effects on melatonin and the extension of the lifetime of radicals can explain the link between EMF exposure and the incidence of for example leukaemia, the two additional mechanisms described here specifically for mouse macrophages, can explain the possible correlation between immune cell system stimulation and EMF exposure. J. Cell. Biochem. 93: 83–92, 2004.

Key words: ELF EMF; free radicals; melatonin

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The question whether electromagnetic fields (EMFs) induce biological effects which might be harmful to human health and the environment remains a controversial issue. Of interest is the exposure to structures and appliances that emit in the extremely low frequency (ELF) range of the electromagnetic spectrum, such as power lines and ordinary household appliances, as well as the emission coming from communication devices using the radiofrequency part of the spectrum (e.g., mobile phones and their base stations). Numerous investigations have shown the presence of a multitude of biological effects, from whole organisms down to the sub-cellular level. However, the situation regarding more specific health effects is not that clear.

Expert groups have recently classified ELF electric and magnetic field exposure as a possible carcinogen, class 2B [NIEHS, 1998; IARC, 2002]. This is primarily based on the risk for childhood cancer and living close to powerlines, and on occupational exposure and an increased risk for leukemia and brain tumors.

Although a large number of reports have been published regarding biological effects caused by power line-frequency EMFs (50/60 Hz) during the last few years [NIEHS, 1998; IARC, 2002, for extensive reviews], there is still need for more basic research in this area, since knowledge of the underlying molecular mechanisms will allow an estimate of potential health risks. The question whether EMFs cause neoplastic development leading to carcinogenesis is of special interest.

However, the basic interaction mechanisms between these relatively weak fields and living matter are presently unclear. Numerous hypotheses have been put forward, although none is convincingly supported by experimental data. There is, furthermore no model for the biological mechanism(s) involved, although our own work, among many others, support that molecules (yet unidentified) in or close to the plasma membrane are involved very early on in the biological response.

There are many observations of cellular responses induced by EMFs in vitro. A large number of cellular components, cellular processes, and cellular systems can conceivably be affected by EMF exposure. However, because evidence from theoretical and experimental studies suggest that EMFs are unlikely to induce DNA damage directly, most studies have been conducted to examine EMF effects on the cell membrane level, general and specific gene expression, and signal transduction pathways. In addition, a large number of studies have been performed on processes such as cell proliferation, cell cycle regulation, cell differentiation, metabolism, and various physiological characteristics of cells. In addition to studies with observed effects after EMF exposure, it must be taken into account that several observations have been difficult to replicate in other studies, and that many studies have reported no effects due to exposure.

It is generally accepted that 50/60 Hz EMF do not transfer energy to cells in sufficient amounts to directly damage DNA leading to genotoxic effects. However, it is possible that certain cellular processes altered by exposure to EMF, such as free radicals, indirectly affect the structure of DNA causing strand breaks and other chromosomal aberrations, including sister chromatid exchange, micronucleus formation, effects on DNA repair, or leading to cytotoxic effects inducing cell death. Genotoxic effects after EMF exposure, such as micronucleus formation in vitro [Simkó et al., 1998a,b, 2001a], chromosomal aberration [Nordenson et al., 1994] or sister chromatid exchange [Rosenthal and Obe, 1989; Khalil and Quassem, 1991] and chromosomal breaks [D'Ambrosio et al., 1988] were reported by different authors. After using the comet assay, dose-dependent DNA strand breaks have been noted [Lai and Singh, 1997; Ivancsits et al., 2002]. In contrast, a number of other studies reported that EMF exposure does not induce chromosomal damage in vitro [Garcia-Sagredo et al., 1990; Livingston et al., 1991; Scarfi et al., 1993; Fairbairn and O'Neill, 1994].

Numerous studies have addressed the interaction between EMF and calcium fluxes, because calcium is a principal regulator of several cellular processes. Modulations in intracellular Ca^{2+} concentrations during exposure to EMF were reported by various investigators [Liburdy et al., 1993a; Lindström et al., 1993; Löschinger et al., 1999; Mattsson et al., 2001]. It has been concluded that modulation of intracellular Ca^{2+} concentrations is possible only in stimulated immune cells [Walleczek, 1992].

In accordance, findings regarding effects on signal transduction processes have also been reported [Korzh-Sleptsova et al., 1995; Uckun et al., 1995; Dibirdik et al., 1998, among others]. This also includes stimulation of activity of the

enzyme PKC, which plays a key role in transferring external signals to the cells interior in order to regulate proliferation and differentiation, as well as other processes. When PKC is activated either naturally or synthetically (e.g., with the phorbol ester TPA), the enzyme is translocated from the cytosol to the cell membrane. Several studies with 50/60 Hz MF on different human cells have shown that treatment with suboptimal TPA concentrations is augmented by EMF exposure, whereas EMF in itself do not cause PKC translocation [Tuinstra et al., 1998; Tao and Henderson, 1999; Richard et al., 2002]. A possible explanation for these results is that cells exposed to suboptimal concentrations of TPA shift from a normal into an activated state without saturating the physiological capacity to respond to TPA, so allowing an additional effect caused by magnetic field exposure.

Alterations in DNA and RNA synthesis rates were found to be produced by EMF; effects on specific gene transcription have also been reported [cf. Lacy-Hulbert et al., 1998]. On the other hand, certain results have not been possible to reproduce at other laboratories, causing intense discussion about the generality of the observations [Lacy-Hulbert et al., 1995; Saffer and Thurston, 1995].

Increases in ornithine decarboxylase (ODC) activity in cultured mammalian cells after exposure to EMF, were reported by several authors [Litovitz et al., 1991; Valtersson et al., 1997; Mullins et al., 1999]. This is of interest since this enzyme is the first and rate-limiting step in the synthesis of polyamines, multicharged low-molecular weight compounds involved in cell growth.

Altered proliferation of cells after EMF-exposure has been observed in a number of studies in vitro. An increase in cell cycle progression of human lymphocytes exposed to a 5 mT (50 Hz) were shown [Rosenthal and Obe, 1989; Antonopoulos et al., 1995] and West et al. [1994] demonstrated increased colony growth in anchorage-independent JB6 cells after 10–14 days exposure to a 1.1 mT (60 Hz) MF. In a study by Katsir and Parola [1998], an increase in cell proliferation with exposure over the frequency range of 50–100 Hz and intensity range of 0.1–0.7 mT was demonstrated. Both frequency- and intensity-dependent responses were observed, with a maximum enhancement of proliferation of 70% seen with exposure to 100 Hz at 0.7 mT. Studies have shown the proliferative effect of EMF with regard to specific cell cycle parameters. In general, these data are consistent with a small decrease in the rate of progression through the early part of the cell cycle. Cridland et al. [1999] revealed that exposure to weak MF (50 Hz, 20 and 200 μT) lead to a delay in the onset of DNA synthesis in synchronized normal human fibroblasts, which indicates a lengthening of the G1 phase. Schimmelpfeng and Dertinger [1993] reported that exposure to 50 Hz, 2 mT caused alterations of several indicators of cell proliferation, including an accumulation of G1 phase cells. Lange et al. [2002] showed that exposure to EMFs (1 mT) modifies the passage of amniotic fluid cells through the cell cycle, leading to a retardation of DNA synthesis, which was indicated by a less rapid increase in the rate of BrdU incorporation. They also described alterations in the expression of cell cycle relevant proteins (cyclins, cdks, p21, p16).

However, in other studies no or opposite effects were found. Zhao et al. [1999] failed to demonstrate any significant differences in the rate of DNA synthesis after EMF exposure (60 Hz, 0.1–0.8 mT) in INIT/10T1/2 cells. Results of Wei et al. [2000] suggest that 60 Hz magnetic fields at intensities of 90 and 120 μT, respectively, can increase [^{3}H] thymidine incorporation into DNA of astrocytoma cells in a time dependent manner, while 60 μT had no effect on the DNA synthesis.

There are several studies concerning cell differentiation under EMF-exposure conditions. Rodemann et al. [1989] described that long-term EMF exposure of fibroblasts in vitro induces the differentiation of mitotic to postmitotic cells that are characterized by differentiation-specific proteins and differentiation-dependent enhanced metabolic activities. Landry et al. [1997] showed that EMFs can affect osteogenesis by increasing the rate of differentiation, whereas Tao and Henderson [1999] reported that only co-exposure to EMF and a phorbol ester (TPA) influence the time-schedule of differentiation in HL-60 cells. A flux density dependent inhibition of differentiation coupled with an increased proliferation rate in the undifferentiated Friend erythroleukemia cells was presented by Chen et al. [2000].

It has been suggested that cells respond to EMF as to an unspecific stressor, causing onset of transcription, and subsequent translation, of

inducible heat shock protein genes (including hsp70) or of heat-shock transcription factor (hsf1) [Goodman and Blank, 1998; Lin et al., 1998; Junkersdorf et al., 2000].

Taken together, these and other studies have shown that the wide variety of effects of EMF exposure on different cell types are dependent on cell age, differentiation status, activation and/or metabolic state, etc. [see also Eremenko et al., 1997; Nindl et al., 1997; Simkó et al., 1998a]. Moreover, the fact that most of the observed effects are of a very small magnitude (often in the order of 20–30%) additionally complicates the evaluation of the controversial results and the verification of published studies.

The aim of this article is to present a hypothesis of a possible initial cellular event affected by exposure to ELF EMF, an event which is compatible with the multitude of effects observed after exposure. The interaction of EMF with the biological system must include activation of a cellular process, which is generally occurring, and capable of activating signal transduction pathways that are causing the previously mentioned observations. Based on several lines of investigations, we here suggest that ELF EMF exposure is able to perform such activation by means of increasing levels of free radicals. Such a general activation is compatible with the diverse nature of observed effects, and is furthermore not excluding other initial interaction processes, possibly due to EMF with other physical characteristics. A considerable amount of the literature supporting this notion relates to experiments on cells of the immune system, which is covered in the next section of this article.

IMMUNE CELL ACTIVATION

Cell regulatory processes, involving the induction of free radical production, which are able to interact with DNA or other cellular components, can lead to a potentiation of free radical-dependent effects. Such processes can therefore be likely targets of EMF-induced cellular responses. In macrophages, physiological activation is associated with the onset of phagocytosis and leads to increased formation of reactive oxygen species (ROS). EMF has been shown to increase ROS levels in phorbol ester-activated neutrophils [Roy et al., 1995], but until recently it was unclear whether non-activated macrophages can be activated by short-term EMF stimulation. Thus, Simkó et al. [2001b] found that 1 mT MF for 45 min is able to activate macrophages and to increase the internalization rate of latex beads with 35%. Particle uptake was measured as a function of flux density, showing a significant increase at doses as low as 0.5 mT. In a previous study [Flipo et al., 1998] using pre-stimulated cells, a decrease in phagocytic uptake of beads combined with increased intracellular Ca^{2+}-levels was reported. However, in this study cells were exposed to static and much higher (25–106 mT) magnetic fields, as well as for prolonged periods of time (24 h).

It is not known why various cell types respond to EMF with different efficacy, but it seems to be clear that several cell types are responsive to EMF by different mechanisms. The responsiveness might depend on the number and the distribution of cell-specific membrane receptors, which are variably expressed on different cell types. It is known that TPA enhances the stimulation of macrophages for phagocytosis via the phospholipid dependent protein kinase C pathway. It is noteworthy that the TPA-effect on differentiation of HL-60 cells was reported to be mimicked by EMF [Tao and Henderson, 1999], similar to the TPA-effect on activation of macrophage phagocytosis in the study of Simkó et al. [2001b].

ROS are unstable reactive molecules produced continuously in several cell types, and are involved in intracellular signal transduction pathways, regulation of gene expression determining the anti-inflammatory response, cell growth, differentiation, proliferation and stress response. A significantly increased super oxide production in the absence of phagocytic activity was detected after exposure to EMF in mouse macrophages [Simkó et al., 2001b; Rollwitz et al., 2004] and also in human monocytes [Lupke et al., 2004], which is an indication of cell activation processes. These investigations demonstrate a low, but significant induction of super oxide production indicating a specific activation of the NADH-oxidase after EMF-exposure. On the other hand, the activation of NADPH-oxidase would result in a higher production of free radicals leading to an oxidative burst. Interestingly, Roy et al. [1995] reported an increased oxidative burst after exposure to 0.1 mT MF in TPA-activated rat peritoneal neutrophils; however the authors proposed an increased lifetime of free radicals due to the magnetic fields as a possible mechanism.

SYNTHESIS AND PROPOSAL OF A HYPOTHESIS

The experimental set-up of the exposure conditions to investigate the influence of EMF on biological systems and its biological effectiveness, are extremely heterogeneous, regarding the field strength, frequency, and the use of pulsed or modulated fields. However, therapeutic application of EMF ranges from bone fracture healing up to cancer treatments [Glaser, 1992] and, therefore the question whether EMFs are biologically effective can be answered with yes. Nevertheless, the nature of the underlying mechanism and their relevance to health risk has to be revealed. It should be taken into account that continuous environmental exposure to 50 Hz EMFs is well below 50 μT, whereas most of the experimental work and all of the medical applications use field strengths beyond 50 μT.

There are several reports published to elucidate possible correlation between EMF and cancer or other diseases but no causal relationship is supported by the discussed mechanisms. Valberg et al. [1997] outlined five main physical possibilities of interaction: (1) energy transfer by acceleration of ions and charged proteins modifies cell membranes and receptor proteins. However, 50 Hz EMF energies are far below those of biomolecules. (2) Electric fields induced inside the body exert forces on electric charges and electric moments, but these forces seem to be smaller than biological forces. (3) Magnetic moments of ferromagnetic particles and free radicals interact with EMF physically, but magnetic field sensory cells have not been found in humans and modification of radical recombination rates in biological systems are very problematic. (4) Resonant interactions include EMFs driving transitions in ion-biomolecule complexes. This mechanism conflicts with accepted physics and experimental tests failed to find effects. (5) Temporal averaging or spatial summation can improve the ratio of signal to noise in any system but this requires structures and processes having the capabilities of EMF detection that have been not found in humans.

It seems that the interaction between EMF and cellular systems is not based on only one of the mentioned hypotheses. Moreover, multiple triggering events seem to amplify cellular reactions, causing different effects, depending on the affected cell type. Externally applied EMFs are able to shift the equilibrium distributions of ions slightly, as described by Blank [1988] in his surface compartment model. Small deviation of the local concentrations near membrane associated enzymes and proteins may trigger their function and induce connected cascades.

The combination of different biological conditions and physical parameters may result in "multiple windows" which interact by secondary mechanisms causing cellular responses that lead to, for example, genotoxicity or other cellular changes. The cell shape seems also to be of importance, for example, fibroblast cells are spindle-shaped whereas blood cells are round in shape. The induced electric fields can be focused in different regions on the cell surface or within the cell causing "hot spots" with very high electric field intensities. Depending on the orientation of exposed cells to the E-field, identical physical parameters can induce different cellular responses [Bernhardt, 1979].

The induced field densities or magnetic fields can influence enzymatic activities by mimicking receptor binding, which affects proteins and other biomolecules to activate biochemical cascades and "out of schedule" cellular reactions. These induced physiological reactions cause cellular effects through secondary or indirect mechanisms such as "cell activation" processes, for example, through the release of free radicals and/or the out of schedule switching-on of transduction pathways.

It has been hypothesized by Stevens [1987] that exposure to 50/60 Hz EMF may suppress the nocturnal production of the pineal hormone melatonin. A later report suggests that reduced levels of melatonin could lead to an increased risk of breast cancer [Stevens and Davis, 1996]. A number of studies have been done to elucidate the role of melatonin and the mechanism of its physiological activity. Melatonin acts also as a receptor independent free radical scavenger and antioxidant, and is able to reduce the incidence of mutations and likelihood of developing cancer. Moreover, melatonin inhibits the growth of different types of established tumours [Dubocovich, 1995; Reiter, 1997]. It seems that melatonin inhibits mammary tumour genesis in animals and in vitro, and acts in an oncostatic manner in different cancer cells [Reiter, 1997]. Several studies described reduced levels of melatonin in EMF exposed animals [Kato et al., 1994; Yellon, 1994] as well as in vitro

[Lerchl et al., 1991; Liburdy et al., 1993b; Löscher and Mevissen, 1994], but short-term exposure to human volunteers failed to provide evidence for EMF-effects on melatonin [Graham et al., 1996; Selmaoui et al., 1996]. However, epidemiological studies reported suppressed levels of melatonin in occupational or residential EMF exposed humans [Pfluger and Minder, 1996; Burch et al., 1998]. It remains to be determined whether EMF exposure is able to reduce the melatonin synthesis or its physiological effects to levels where an increased cancer incidence would be a consequence.

In order to clarify the question of a possible correlation between cancer and EMF, reproducible effects at the cellular level have to be obtained and the underlying mechanisms have to be elucidated. It is important to note that most experimental designs of EMF exposure and hence investigations are focused only on simple well defined questions. However, the interaction of EMF with an organism is very complex. We, therefore set out to describe mechanisms, which take into account the whole organism.

We have shown in previous studies that 50 Hz EMF induce genotoxic effects in human amniotic cells. However, it is obvious that EMFs are not able to induce genotoxic effects by direct interaction with DNA, but only due to an indirectly mediated mechanism. The shape, origin, and the amount of cell-specific membrane receptors seem to play a key role in the effectiveness of EMF. Depending on the receptors, cell specific responses can be induced, leading to cell specific activity.

We also studied the PKC mediated signal transduction pathway in human amniotic fluid cells, in SCL II cells as well as in mouse bone marrow derived macrophages and did not find any direct correlation between EMF-exposure and PKC activation [Simkó et al., 2001b; Richard et al., 2002]. However, further studies at the molecular level showed disturbances and changes in the expression of cell cycle related proteins [Lange et al., 2002]. Therefore, we conclude that genotoxicity after exposure to EMF is due to secondary induced mechanisms, such as, the production of free radicals, which must be induced by different signal transduction pathways.

Free radicals are important intermediates in natural processes and are released during natural cell metabolism. These intermediates arise in mitochondrial respiration and are also a key feature of the phagocytic process. It is well known that the release of free radicals is inducible by ionizing radiation or TPA, both leading to genomic instability. EMF might be a stimulus to induce cell activating processes causing an "activated state" of the cell such as in phagocytic activity, which then enhances the release of free radicals, which in turn can lead to genotoxic events.

Scaiano et al. [1994] proposed that MF is able to stabilize free radicals in such a way as to increase their lifetime and permit a wider dispersion rather than their return to the basal level. The hypothesis of a prolonged lifetime of free radicals will increase the probability of radical-mediated DNA damage and therefore the overall amount of DNA damage, leading to clastogenic damage. The suppression of the EMF enhanced cell proliferation in the presence of radical scavengers, shown by Katsir and Parola [1998], is another supportive finding for this proposed model of interaction between EMF and biological systems.

Macrophages play an essential role in the immune system. Activated macrophages possess enhanced phagocytosis and elevated physiological production of toxic oxygen as well as nitrogen intermediates. In our studies, an increased phagocytic activity in mouse macrophages after exposure to EMF was detected in a dose-dependent manner [Simkó et al., 2001b]. This cellular activation was shown in the absence of any pre- or co-stimulation. We, furthermore showed increased super oxide radical production during exposure to 1 mT EMF in the absence of phagocytosis. This is taken for evidence of a direct activation of macrophages by EMF.

Tan et al. [1999] identified markedly elevated levels of melatonin in rat bone marrow, which is an endogenous free radical scavenger and an immune-enhancer. It has been suggested that the high level of melatonin may provide protection by reducing oxidative damage and to enhance the immune capacity. Therefore, melatonin is supposed to be oncostatic as well. As it has been hypothesized that EMF may suppress melatonin synthesis [Stevens and Davis, 1996], reduced levels of melatonin could also lead to an increased cancer risk. The following reaction may be induced in an organism after chronic exposure to EMF: an increased "cell activation" process concomitant with an increased free

radical production including a prolonged lifetime of radicals, coupled with a decrease of the radical scavenger melatonin leading to increased ROS levels in organs generally, but especially in lymph nodes and in the bone marrow including stem cells. Such changes could lead to an increased risk of cancers such as lymphomas and leukemia, but also to breast cancer. On the other hand, short term exposure to EMF may have the beneficial effect of activating immune response cells such as macrophages. These findings have potential implications for therapeutic applications.

The different pathways of free radical involvement in physiological and pathological reactions to EMF exposure are summarized in Figure 1. The hypothesis how cancer can be induced or promoted in macrophages is one example of cell activation processes by EMF. Direct activation of macrophages (or other cells) by short-term exposure to EMF leads to phagocytosis (or cell specific response) and consequently, free radical production (a). This pathway may be utilized to positively influence certain aspects of the immune response, and could be useful for certain therapeutic applications. An additional pathway in EMF-induced macrophage (cell) activation is the direct stimulation of free radical production (b). The documented increase in the lifetime of free radicals by magnetic fields [Walleczek, 1992; Harkins and Grissom, 1994; Roy et al., 1995] leads to elevated free radical concentrations for extended periods of time (c). In general, reactions in which radicals are involved become more frequent, increasing the possibility of DNA damage. The fourth pathway (d) suggested, leading to an increase of free radical concentration, is the inhibitory potential of chronic EMF-exposure on the availability of the pineal gland hormone melatonin [Thun-Battersby et al., 1999; Caplan et al., 2000], which acts as a radical scavenger. Such reduced melatonin levels could be involved in amplification of DNA damage.

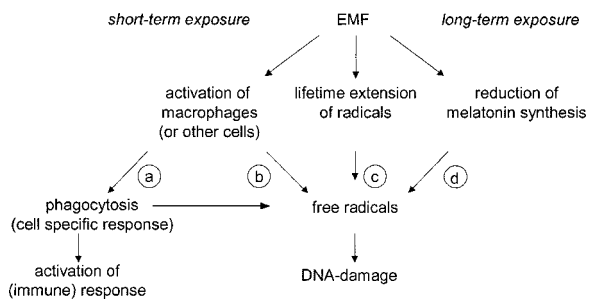

Fig. 1. Pathways of ROS involvement in cellular reactions subjected to short- and long-term EMF exposure. Stimulation of the immune system through macrophage activation is a favourable response to short-term EMF-exposure (**a**). Free radical production may arise directly from macrophage or other cell specific activation (**b**) or radical lifetime extension (**c**). Similarly, increase of ROS has been attributed to the inhibiting capacity of EMF on the availability of the pineal gland hormone melatonin which is a known scavenger for free radicals (**d**) after long-term EMF-exposure.

Altogether, these EMF induced reactions could lead to a higher incidence of DNA damage and therefore, to an increased risk of tumour development. While the effects on melatonin and the extension of the lifetime of radicals have been invoked to explain the link between EMF exposure and incidence of for example, leukaemia and mammary gland tumours, the two additional mechanisms described here specifically for mouse macrophages can well explain the possible correlation between immune cell system stimulation and EMF-related tumour development. Thus, tumours developing from tissues affected by chronic inflammatory diseases as well as leukaemias and lymphomas have in common that a higher number of activated radical-producing macrophages are residing in the vicinity of their origin. On the other hand, the potential for employing short-term EMF exposure for therapeutic purposes is obvious and should be further explored.

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