THE BIOLOGICAL INFLUENCES OF LOW-FREQUENCY SINUSOIDAL ELECTROMAGNETIC SIGNALS ALONE AND SUPERIMPOSED ON RF CARRIER WAVES

Carl F. Blackman

Health Effects Research Laboratory
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Interest in the biological effects of low frequency modulation of RF radiation stems from reports of changes caused by exposure to electric and magnetic fields in the sub-ELF range (0-30 Hz). It has been reported that exposure to low-frequency electric fields changes the reaction time in humans (Konig and Ankermuller 1960, Hamer 1968, Konig 1971) and in monkeys (Gavalas et al. 1970; Gavalas-Medici and Day-Magdaleno 1976), and alters circadian activity in human beings (Wever 1973). Friedman et al. (1967) observed that magnetic fields modulated at low frequencies also change reaction time in human beings.

Two other studies that provide important background information are Kaczmarek and Adey (1973, 1974). In the first report, they described release of calcium ions and gamma-aminobutyric acid (GABA) from the cerebral cortex of cats in response to small changes in the extracellular concentration of calcium. In 1974, they demonstrated release of calcium ions and GABA from the cat cortex in response to low intensity electric currents, pulsed at 200 Hz, applied directly to the cerebral cortex. Thus, extracellular calcium and electric current have similar effects on the release of GABA and calcium ions from brain tissue.

The studies of (1) behavioral changes in animals and human beings induced by low frequency signals and (2) biochemical changes in the cat brain caused by electric currents led to a study of the influence of electric fields on EEG patterns associated with a conditioned behavioral response in cats (Bawin et al. 1973). To increase the penetration of the signals into the tissue, they chose an RF carrier wave of 147 MHz, which was amplitude modulated in the sub-ELF range (e.g., 3-14 Hz). Alterations were observed in the rate of performance, accuracy of reinforced patterns, and resistance to extinction in learned behavior of the exposed animals compared to controls, indicating that the fields were acting as reinforcers. In order to determine whether these effects were mediated via peripheral receptors or occurred as a result of changes induced directly on the CNS, experiments were designed to examine the effects of modulated RF carrier waves on brain tissue in vitro.

CALCIUM ION EFFLUX IN VITRO: A FUNDAMENTAL FINDING

The association of calcium ions with brain tissue was selected as the biochemical marker to examine the influence of modulated RF fields because calcium ion efflux had been shown to be sensitive to electric currents applied directly to brain tissue in vitro, and because calcium ions have a prominent role in many biochemical and biophysical processes (e.g., cellular membrane integrity and function, enzyme cofactor, putative second messenger for the conduction of extracellular signals to the nucleus of the cell, neural tissue excitation and secretion of transmitter substances at synapses). The first report of the influence of modulated RF fields on excised brain tissue was Bawin et al. (1975), who showed that a 20-min exposure of chick brain tissue in vitro to a 147-MHz field at 1 to 2 mW/cm^2 (SAR estimated at 0.002 W/kg) caused enhanced efflux of calcium ions, but only if the field was sinusoidally amplitude modulated at frequencies of 6, 9, 11, 16, or 20 Hz. Maximal efflux was measured at 16 Hz. Modulation frequencies of 0, 0.5, 3, 25, and 35 Hz were ineffective. This frequency-specific response, which occurred while the 147-MHz carrier field was maintained at the same power density, indicates that the field-induced efflux of calcium ions was not due to heating of the samples.

In another report, Bawin et al. (1978a) exposed chick brain tissue for 20 min to 450-MHz fields, amplitude modulated at 16 Hz, at 0.75 mW/cm^2 (SAR estimated at 0.0035 W/kg) under a variety of chemical conditions. The results demonstrated that a) the enhanced efflux of calcium ions is not highly sensitive to the external calcium concentration, b) bicarbonate appears to be important for enhanced efflux, c) lowering the pH from 7.6 to 6.8 in the presence of bicarbonate may enhance the magnitude of efflux, and d) lanthanum causes a reversal to field-induced retardation of calcium-ion efflux.

Corroboration of the frequency-specific response described by Bawin and co-workers was provided by Blackman et al. (1979) who showed that 16-Hz amplitude modulation of 147-MHz carrier waves caused enhanced efflux in chick brain tissue in vitro, while modulation frequencies of 3, 9, and 30 Hz did not. Although the data had large variances, an unusual intensity response was described, i.e., only 0.83 mW/cm^2 (SAR estimated at 0.0014 W/kg) produced a statistically significant efflux enhancement (intensity values are corrected based on discussion in Blackman et al. 1980a) while power densities (0.11, 0.55, 1.11 and 1.38 mW/cm^2) below and above the effective value did not cause efflux. In a later report, Blackman et al. (1980a) used a revised statistical model and experimental procedure to reduce the influence of the large sample variance. An intensity response identical to their earlier result was found. However, when the distance between samples was halved, the range of intensities that produced enhanced efflux increased to include 0.55, 0.83, 1.11 and 1.38 mW/cm^2, whereas lower and higher values of 0.11 and 1.66 mW/cm^2 were ineffective. In addition, an intensity region from 0.55 to 1.11 mW/cm^2 caused enhanced efflux when 9 Hz was used as the modulation frequency. These data, obtained with a more rigorous experimental protocol, provided additional support for the results of Bawin et al. (1975) and Blackman et al. (1979); however, the explanation for the dependence on sample spacing awaited further developments.

Joines et al. (1981) examined the dependence on sample spacing by calculation of the electrical coupling between the samples; for simplicity the samples were modeled as spheres. They found that increased electrical interaction between the more closely-packed spheres produced a broader range of internal field strengths within each sphere. Thus, if a given internal field strength were necessary to cause enhanced efflux, there is a greater chance for that internal field strength to occur in closely-coupled samples exposed to a specific range of incident intensities. Joines et al. (1981) found this result to be consistent with the experimental findings in Blackman et al. (1980a). Thus a potential artifact was shown to be a logical result of the experimental procedures.

The intensity response observed by Blackman et al. (1979) with modulated 147-MHz carrier waves was confirmed by Sheppard et al. (1979) with 450-MHz carrier waves, modulated at 16 Hz; calcium-ion efflux was enhanced at 0.1 and 1.0 mW/cm^2 but not at 0.05, 2.0 or 5.0 mW/cm^2 (the estimated SAR at 1.0 mW/cm^2 is 0.0047 W/kg). The results of these two reports show that the intensities producing calcium-ion efflux from chick brain tissue *in vitro* are within the range of 0.1 to 1.38 mW/cm^2 for modulated 147-MHz and 450-MHz carrier waves.

The apparent carrier-frequency independence of effective intensities was tested with a 50-MHz carrier wave, amplitude modulated at 16 Hz. Enhanced efflux of calcium ions from brain tissue occurred within two intensity regions (between 1.44 and 1.67, and at 3.64 mW/cm^2; SAR's <0.0035 W/kg) separated by intensities of no effect including 0.72 mW/cm^2 (Blackman et al. 1980b). These effective intensity values were different from the corresponding values of 147-MHz radiation; thereby indicating a dependence on carrier frequency. In addition this result revealed the existence of more than one range of effective intensities.

The apparent discrepancy in effective power densities at the three different carrier frequencies (50, 147 and 450 MHz) has been resolved by the finding that efflux is dependent on the electric field strength within the tissue and not on incident intensity (Joines and Blackman 1980). The calculation to transform the incident intensity to internal field strength was based on an empirical model described by Joines et al. (1981). With the data available at 50 and 147 MHz, the model was used to predict intensities that would produce both alterations and no alterations in calcium-ion efflux; some predictions were tested and found to be valid (Blackman et al. 1981). These reports described two intensity ranges that appear effective for enhanced efflux at both 50 and 147 MHz, identified the internal electric field strength rather than incident intensity as the important exposure parameter, and showed the importance of frequency-dependent complex permittivity values of brain tissue in the conversion of incident intensity to internal field strength. The exposures at 50 and 147 MHz caused no generalized heating of the sample. The maximum temperature rise was calculated to be <0.0004 °C, and calculated SAR's at each carrier frequency were <0.0014 W/kg (Blackman et al. 1980b).

Subsequent to the critique by Athey (1981) that the simple spherical model used by Joines and Blackman (1980) was too idealized, these authors showed that a layered sphere model produced relationships between incident intensities at 50, 147 and 450 MHz and internal field strengths that were also consistent with the experimental results (Joines and Blackman 1981). The success of the initial, simple models to predict intensity regions of both field-induced efflux enhancement and no enhancement demonstrates the utility of the approach. More refinements in the models are necessary before the experimental situation is realistically described. For example, Blackman and Wilson (1983) using autoradiographic techniques established the distribution and penetration of radioactive calcium ions in chick brain tissue immediately prior to exposure to electromagnetic fields. They concluded that the radioactive label penetrated by diffusion and that there was no label greater than 1 mm from the surface. This result agrees with previous work indicating that the radioactive label only penetrated to the outer 1 mm of the tissue (Adey et al. 1982). Thus, refinements to the mathematical models should focus on conditions that occur at or near the tissue surface.

Two ancillary experiments were performed by Blackman et al. (1981). In one, they reported that the presence of the bicarbonate buffer component was essential in potentiating enhanced calcium-ion efflux due to electromagnetic radiation. When Tris or HEPES buffers were substituted for bicarbonate, they failed to observe changes in radiation-induced efflux. They also reported that Bawin, in a personal communication, had failed to detect radiation-induced changes when bicarbonate was replaced with imidazole or MOPS buffers. In the second experiment, they examined the metabolic state of the brain tissue and found that substantial respiratory activity lasted through the 55- to 60-minute experimental period, although freshly excised tissue exhibited slightly higher respiratory rates.

Shelton and Merritt (1981), who used different procedures from those described by Bawin et al. (1975), Blackman et al. (1979, 1980a,b), and Sheppard et al. (1979) reported no change in calcium ion efflux from rat brain. Brain tissue slices, labeled _in vitro_ with radioactive calcium, was irradiated at 1-GHz, pulse-modulated with square waves at 16 or 32 Hz (0.5, 1.0, 2.0 and 15 mW/cm^2). In a second report, Merritt et al. (1982) exposed rat brain tissue labeled _in vivo_ with radioactive calcium to microwave radiation, pulse modulated at 16 Hz (20-ms pulse width). The intensities for the 1-GHz carrier frequency were 1 mW/cm^2 (SAR = 0.29 W/kg) and 10 mW/cm^2 (SAR = 2.9 W/kg); and for the 2.45-GHz carrier frequency, 1 mW/cm^2 (SAR = 0.3 W/kg). In addition, animals labeled with radioactive calcium were exposed for 20 min to 2.06-GHz radiation at one of 17 different combinations of intensity and pulse repetition rate: 0, 0.5, 1.0, 5.0, 10.0 mW/cm^2 (SAR was 0.24 W/kg per mW/cm^2), and 0, 8, 16, 32 Hz (pulse width was 10 ms). Following exposure, brain tissue was analyzed for radioactivity. No statistically significant field-induced enhancement of calcium-ion efflux or change of calcium content in the brain tissue was found. The reason for these negative findings is not known; however, the use of square wave rather than sine wave modulation, the different biological preparation, and different medium composition are factors that may have influenced the outcome.

ADDITIONAL CNS STUDIES

The reports of field-induced calcium-ion efflux from chick brain tissue _in vitro_ have led to other CNS studies. Synaptosomes, prepared from rat cerebri and labelled with radioactive calcium, were exposed for 10 min at 0.5 mW/cm^2 to 450-MHz fields, amplitude modulated at 0, 16, or 60 Hz (Lin-Liu and Adey 1982). Only 16 Hz affected the efflux kinetics of calcium ions. The exact SAR while low, can not be unequivocally established because the exposure chamber may have been operated in a multi-modal condition (see Weil et al. 1981). Nevertheless, this result is modulation dependent and it is unlikely that heating is involved as a causative agent.

Similar field-induced efflux enhancement has been reported in a live animal. Adey et al. (1982) exposed awake, immobilized cats to 450-MHz fields, amplitude modulated at 16 Hz, at 3.0 mW/cm^2 (SAR = 0.29 W/kg). The release of calcium ions from the cortex was observed as a function of time. Irradiation for 60 min caused episodes of enhanced efflux lasting 20 to 30 min and extending into the post-exposure period. Although focusing on a different component of the efflux kinetics than studied by Lin-Liu and Adey (1982), these results demonstrate that RF fields modulated at 16 Hz can cause changes in both a subcellular membrane system and in the live mammal. Thus, the field-induced phenomenon is not restricted to an avian species nor to *in vitro* preparations.

Recently, Dutta et al. (1984) observed field-induced enhancement of calcium ions from cells of human origin. Monolayer cultures of human neuroblastoma cells were exposed for 30 min at ten SAR's from 0.01 to 5.0 W/kg to 915-MHz fields, with or without sinusoidal amplitude modulation (80%) at frequencies between 3 and 30 Hz. Significant increases in the efflux of calcium ions occurred at two SAR's (0.05 and 1.0 W/kg). The increased efflux at 0.05 W/kg was dependent on the presence of 16-Hz modulation but not at the higher value. Exposure at modulation frequencies between 3 and 30 Hz (SAR = 0.05 W/kg) revealed a peak in the response at 16 Hz. Although the effective SAR (0.05 W/kg) for 16 Hz modulation is over 38 times larger than the SAR's for enhanced efflux of calcium ions from chick brain tissue *in vitro*, the low frequency response pattern was similar to that reported by Bawin et al. (1975) and Blackman et al. (1979). The relation of enhanced efflux with unmodulated fields at 1.0 W/kg with the effects of modulated fields is not known at this time; however, it is not due to a temperature increase in the sample because enhancement was not found at SAR's of 2.0 and 5.0 W/kg.

The effect of modulated RF fields on the EEG was investigated by Takashima et al. (1979). Rabbits were exposed 2 h daily for six weeks to 1.2 MHz, amplitude modulated at 15 Hz, or 5 MHz amplitude modulated at 14 Hz. Following exposure, the EEG was recorded with scalp electrodes and, when compared to the pre-treatment EEG pattern, was found to be altered with enhanced low-frequency components and decreased high-frequency components. The EEG pattern returned to the pre-treatment pattern after several weeks post-exposure. Although the electric field intensity was given as 500 V/m, with an error factor as large as two, the important aspect of the results was that unmodulated fields of similar intensity had no effect on the EEG pattern. The authors have recently stated that this field-induced change in the EEG pattern proved to be elusive and further study was discontinued because it was beyond the resources of the group. Nevertheless, the absence of metallic electrodes in the animal during exposure avoids the major criticism of earlier studies that reported field-induced changes in EEG patterns (Gavalas et al. 1970, Bawin et al. 1973). Thus, this report stands as an important adjunct to the previous work.

Sagan and Medici (1979) studied the influence of 450-MHz fields, sinusoidally amplitude modulated at either 3 or 16 Hz, on locomotor activity in young chickens. The experiments were performed in a plastic, modified Skinner box with light beams to monitor activity; the complete apparatus was placed in an anechoic chamber and exposed in the far field. The authors found no statistically significant change in performance during or immediately after a 23-min exposure at 1 or 5 mW/cm^2 (SAR estimated at 0.2 and 1.0 W/kg). They concluded that the lack of a field-induced response could be due to the use of modulation frequencies not present in the chicken's EEG during performance on the particular (fixed-time schedule) task. Two alternative possibilities exist: (1) based on the multiple-intensity ranges observed for field-induced calcium-ion efflux, the two intensities used in this study may have been outside the effective ranges, and (2) the appropriate combination of frequency and steady-state magnetic field intensity may not have been used (see below for a more detailed discussion).

In summary, four groups (Adey et al., Blackman et al., Dutta et al., and Takashima et al.) have shown that RF fields, sinusoidally modulated at.sub-ELF frequencies, especially 16 Hz, cause changes in different CNS preparations including the live animal. Many of these studies have been analyzed in reviews (Adey 1981, Blackman et al. 1981, Greengard et al. 1982, Myers and Ross 1981, Postow and Swicord 1985). It is generally agreed that both the mechanism of interaction and the physiological consequences of these changes are yet to be established.

NON-CNS STUDIES

The effect of exposure of pancreatic tissue and T-lymphocytes to RF fields, sinusoidally amplitude modulated at low frequencies, have been examined. An increase of calcium ion efflux from rat pancreatic tissue exposed *in vivo* at 2 mW/cm^2 for 1 to 2.5 h at 147 MHz, modulated at 16 Hz (estimated SAR <0.075 W/kg), has been reported by Albert et al. (1980). However, the efflux was not accompanied by a change in protein secretion which is normally associated with calcium mobilization in the pancreas. The authors attributed the lack of protein secretion to a limitation imposed by the exposure conditions, i.e., a relatively small volume of medium was available to the tissue for normal metabolic activity.

In another *in vitro* assay, the cytotoxic activity of mouse T-lymphocytes was suppressed by a 2-h exposure (1.5 mW/cm^2) to 450-MHz fields, modulated at frequencies between 16 and 100 Hz (Lyle et al. 1983). Peak suppression occurred at 60 Hz modulation, with smaller effects at 16, 40, 80 and 100 Hz. The exposed cells recovered full cytotoxic activity 12.5 h after the termination of exposure. This result demonstrated an inhibitory but reversible effect on a cell-mediated immune response by modulation frequencies.

SINUSOIDAL ELF AND SUB-ELF SIGNALS

Most of the studies reviewed above demonstrate an absolute requirement for low frequency sinusoidal modulation of the RF carrier wave in order for the signal to be effective biologically. There are also reports that describe biological effects of exposure to low frequency electromagnetic signals in the absence of an RF carrier wave. Bawin and Adey (1976, 1977) exposed chick and cat cerebral tissue for 20 min to 1, 6, 16, 32 or 75 Hz at electric field gradients of 5, 10, 56 and 100 Vp-p/m in air. Only two frequencies, 6 and 16 Hz, caused a reduction in calcium ion efflux at 10 and 56 V/m for the chick tissue, and 56 V/m for the cat tissue. Because all other combinations produced no field-induced responses, the authors described "amplitude and frequency windows" for calcium-ion efflux. Electric field gradients within the tissue were estimated to be 10^{-5} V/m. The field-induced reduction in efflux is in contrast to the enhancement caused by modulated RF carrier waves. Nevertheless, the frequency dependence observed in the two studies was similar which suggests an interaction with a common substrate as the site of interaction.

Blackman et al. (1982) used chick brain to study the influence of 16-Hz signals at 15 intensities between 1 and 70 Vp-p/m on the efflux of calcium ions. Two intensity regions that included 5, 6, and 7.5 V/m and 35, 40, 45, and 50 V/m caused enhanced efflux. No field-induced effects were seen below (1, 2, and 3.5 V/m), between (10, 20 and 30 V/m), or above (60 and 70 V/m), the two effective intensity regions. Moreover, 1 and 30-Hz signals at 40 V/m caused no change in efflux. This finding is consistent with the reports of multiple-intensity regions of enhanced efflux caused by modulated RF radiation (Blackman et al. 1980b, 1981). In addition to the intensity response, the frequency dependence corroborated reports by Bawin and Adey (1976) for low frequency signals, and by Bawin et al. (1975) and Blackman et al. (1979) for modulated RF fields.

In these two low-frequency studies, the cause of the slight difference in effective intensities is unknown. The major disagreement in the results of Bawin and Adey (1976) and Blackman et al. (1982) is the direction of the change in efflux; the latter authors state that the "cause may be found in the slightly different preparations and procedures used in the two laboratories."

Blackman et al. (1983, 1985) have extended their low frequency studies to cover the range from 1 to 120 Hz at an intensity of 42.5 Vp-p/m, and over a series of intensities at single frequencies of 42, 45, 50, and 60 Hz. They found intensity ranges at 45, 50 and 60 Hz that caused enhanced calcium-ion efflux from chick brain tissues, while the four intensities tested at 42 Hz were ineffective. In the range from 1 to 120 Hz, two frequency ranges elicited enhanced efflux--one centered on 15 Hz and the other extending from 45 to 105

Hz. The results in this report emphasize the importance of the interrelation between frequency and intensity in establishing exposure conditions that can elicit the biological response. It should serve as a guide for designing future experiments to investigate the biological influence of low frequency electromagnetic signals.

Recently Blackman and co-workers have shown that the intensity of the steady-state (DC) magnetic field of the earth is directly related to the frequencies of the oscillating (AC) EM signal that cause enhanced efflux of calcium ions from the chick brain tissue. The effective frequency was directly proportional to the intensity of the DC magnetic field times an index, $2n + 1$, where $n = 0,1$. A 40 V/m EM signal at 15 Hz, was effective in causing enhanced efflux of calcium ions when the intensity of the DC magnetic field was 38 μT, but not when it was reduced to 19 μT; similarly a 30 Hz signal that was ineffective at 38 μT was effective at ±25.3 μT and at ±76 μT. In all the previous work published by Blackman and co-workers the intensity of the DC magnetic field was 38 μT. Blackman et al. (1984) have shown that the AC magnetic component must be present for a 16-Hz, 40-V/m EM signal to cause enhanced efflux. Because the orientation of the DC magnetic field was always perpendicular to the plane formed by the electric and magnetic AC vectors, there is insufficient information to distinguish between a cyclotron resonance-like mechanism and a magnetic resonance-like mechanism. In the former case, the electric component of the AC signal must be perpendicular to the DC field for maximum coupling; in the latter case, it is the magnetic component that must be perpendicular. The experimental situation at the transduction sites may be too complicated for simple manipulations of the field orientations to resolve this ambiguity. Nevertheless, while these results complicate any theoretical analysis of the calcium-ion efflux phenomenon, they may provide an essential clue not only to the underlying mechanism of action but also to explain why otherwise identical experiments with low frequency electromagnetic signals can produce different results.

Several research groups have reported biological changes induced by low frequency, sinusoidally oscillating magnetic fields. The myxomycete Physarum polycephalum has a longer mitotic cycle and reduced respiration rate after chronic exposure to 2.0 gauss magnetic fields at 75 Hz (Goodman et al. 1979). Human fibroblasts in culture exposed to sinusoidally varying magnetic fields for a wide range of frequencies (15 Hz to 4 kHz) and amplitudes (0.25 to 5.6 gauss) exhibit enhanced DNA synthesis (Liboff et al. 1984). Fruit flies (Drosophila melanogaster) preferred not to deposit eggs in a 10-gauss, sinusoidally varying 50-Hz magnetic field; similar exposure during development of the egg produced less viable eggs and pupae in the exposed samples than in controls (Ramirez et al. 1983). These results suggest that low frequency, sinusoidally varying fields may alter fundamental biological processes.

Low frequency, pulsed magnetic fields have also been reported to produce alterations in diverse biological systems. These systems include the developing chick embryo (Delgado et al. 1982, Ubeda et al. 1983), *Drosophila* egg laying and mortality (Ramirez et al. 1983), the de-differentiating amphibian red blood cell (Chiabrera et al. 1979), transcription in the *Dipteran* chromosome (Goodman et al. 1983), nerve cells in culture (Dixey and Rein 1982), and mouse bone cells in culture (Luben et al. 1982). Many of these studies used an intricate pulsed waveform, which has been used in therapeutic devices for bone nonunions. All the studies used pulse repetition rates below 500 Hz, with most below 100 Hz. It is not known whether these pulsed fields cause alterations via the same mechanism(s) as sinusoidal fields. Recently, Liboff et al. (1984) questioned the need for the particular wave shapes; it appears that the essential element is the low frequency field.

ESSENTIAL STEPS IN A MECHANISM OF ACTION

The field-induced calcium-ion efflux phenomenon can be conceptualized as occurring in a multistep process. The first step is the initial transduction of electromagnetic energy into a chemical change at the primary reaction site. This chemical change would be expected to be small because the electromagnetic signal contains very little energy when compared to thermal energy at 37 °C. Identification of this primary transduction site and the nature of the chemical change are presently unanswered issues. The second step is the amplification of the small chemical change by utilizing energy already stored in the biological system. This amplification process could occur through a cooperative transition, such as a phase change, in which the biological system is energetically poised and needs only a minute change to initiate the transition. The third step is the secondary reactions that ensue as a result of the transition, that cause changes in observable properties, such as calcium-ion association with the tissue surface. These processes may occur within the same molecular species and be experimentally inseparable steps or, in the other extreme, they may occur between different molecular species that are chemically coupled and distinguishable under appropriate conditions. By viewing phenomena induced by ELF signals in this way, it may be possible to resolve apparent similarities and devise appropriate tests to determine whether those similarities represent the products of the same underlying mechanism.

SUMMARY

Many reports of effects of RF fields, amplitude modulated at very low frequencies, have not been independently corroborated. The major exception is calcium-ion efflux from chick brain tissue *in vitro* at intensity levels far below those that cause heating. This exception, combined with the results of studies of brain biochemistry and EEGs in animals and with synaptosomes and human neuroblastoma cells in culture, provides evidence that CNS tissue from several species, including human beings, are affected by low-intensity RF fields sinusoidally amplitude modulated at specific low frequencies or by those low frequencies directly. The responses over several distinct intensity ranges and the recently demonstrated influence of the earth's steady-state magnetic field in the calcium-ion efflux experiments further emphasize the unusual nature of these findings in chick brain tissue. The physiological significance of these field-induced effects is not established.

In addition to the CNS-related changes, amplitude-modulated RF fields have been reported to alter an immune response and a pancreatic tissue function. These reports with diverse biological systems are without apparent connection to each other except for the physical agent causing the change. The critical parameter common to all these experiments is the specificity of the low frequency electromagnetic signal. However, in most cases dose response curves and action spectra, viz. magnitude of the response as a function of frequency, have not been obtained. More detailed parametric manipulation of these factors, with appropriate allowances for the steady-state magnetic field vector, would permit comparisons and correlations between widely differing biological endpoints to assist in focusing on potential common underlying mechanism(s) of action. Unfortunately, this viewpoint is currently not appreciated by researchers who narrowly focus on the biological ramifications in their own specialized systems, in the hunt for the underlying mechanisms and physiological significance. By adopting this approach, they may be missing an opportunity to coalesce the individual efforts and to identify the critical common parameters. Perhaps the discovery of the influence of the steady-state magnetic field will provide a unifying guide for future research.

No report has yet described a mechanism of action in sufficient detail to identify the conditions necessary and sufficient to explain unequivocally calcium ion efflux in the brain or the other biological changes caused by low frequency signals or by modulated RF fields. The response to specific frequencies and intensities is unusual and at present unexplained. This response to amplitude modulated RF radiation or to sub-ELF signals alone may be a true field effect at a very low SAR and at biologically relevant frequencies, i.e., in the range of frequencies normally present in the EEG. The frequency-specific nature of the responses and the involvement of the earth's steady-state magnetic field provide evidence against heat as the underlying cause. The unusual, multiple-intensity-range response challenges standard dose-response analyses, and by its very nature, may prohibit the invocation of threshold levels.

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