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One Year Exposure to Nocturnal 7 Hz, Amplitude-Modulated Magnetic Fields Suppresses Clinical Expression of DMBA-Induced Tumors in Female Rats

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Abstract

Female rats that had received only four oral administrations of Dimethylbenz(a) anthracene (DMBA) were exposed for one year every night for about 6 min every hour between midnight and 08 hr to various intensities of 7 Hz, amplitude-modulated magnetic fields generated through Helmholtz coils. The rats exposed to intensities between 400 and 500 nT did not develop any overt tumors even though they received DMBA. On the other hand rats exposed to the intensities between 30 and 60 nT developed a variety of different, qualitatively unusual tumors that were located within pancreatic, salivatory, and nasal tissues. Their histological features are presented. These results should be considered preliminary but suggest that protracted exposures to particularly patterned and intensity magnetic fields during the nocturnal cycle may suppress the chemical reactions that contribute to the nuclear changes in the cell or the intercellular cohesive networks that ultimately trigger these massive proliferations of tissue.

Keywords: DMBA; Nocturnal magnetic field exposure; 7 Hz amplitude-modulation; Pancreatic tumors; Salivatory tumors; Histology

Introduction

The potential interaction between ambient, biofrequency electromagnetic fields generated by the technologies of western civilization and the biological process that produce malignancy has been supported by a large number of correlation studies and cell-culture research [1]. These investigations have focused primarily upon the influence of 50 Hz or 60 Hz magnetic fields generated by power lines or indirectly from various configurations of wiring [2]. Critical field strengths for increasing the risk of developing some form of cancer relative to a reference group varies with the age of the population and usually involves exposure for several years to intensities greater than about 1 µT (10 mG). There has been substantial variability in the odd ratios for exposed populations as well as effect sizes of the multitude of signaling pathways that are affected within cell cultures. The potential for interaction between pharmacological compounds and whole body exposure to power frequency electromagnetic fields was reviewed by Whissell and Persinger [3]. They suggested that the most challenging problem in the 21st century will be predicting the synergisms between drugs or chemicals consumed inadvertently or purposely by people and the increasingly "bioeffective" electromagnetic matrix produced by industrial and habitat-related power frequencies superimposed upon communication technologies. The latter become relevant when "beat frequencies" within the 1 Hz to kHz range emerge from the GHz and MHz carriers. The inspiration for considering such synergism between an applied, body-permeating electromagnetic stimulus and internal chemical reactions was derived from the powerful effects reported by Thomas et al., [4] when they exposed rats to specific intensities of microwave radiation and a commonly consumed benzodiazepine. Only when the two stimuli were combined was the effect conspicuous. Few experiments [5] have been designed to discern if particular combinations of intensities and frequencies of applied magnetic fields might modify the untoward consequences of oncogenic compounds. If the electromagnetic fields were simulating the types of interactions that occur

between ligands and receptors, very specific parameters would be required to converge with the required energies and temporal patterns for the dynamics between boundaries of reactions. For example in other studies [6,7] we found that female Lewis rats inoculated with a preparation of spinal cord emulsion did not develop experimentally allergic encephalomyelitis as severely if they were exposed continuously to an amplitude-modulated 7 Hz, 50 nT magnetic field for about 6 minutes per hour eight times during the later scotophase. Neither exposures to the same 7 Hz amplitude modulated pattern but with a peak of 500 nT or 40 Hz, 50 nT or 40 Hz, 500 nT configurations impeded the development. The symptoms in rats exposed to these conditions did not differ from non-treated controls.

In the present experiment we combined the treatments with dimethylbenz(a)anthracene (DMBA), a drug known to produce malignancies [8,9], and exposure for one year to the same, intermittently presented (once per hour, 8 times during the night phase), 7 Hz, amplitude-modulated magnetic field. We had selected this frequency based upon the historical literature concerning the importance of the Schumann resonance [10], an intrinsic standing wave generated between the earth and ionosphere and to which all living systems have been exposed since abiogenesis [11]. We have assumed, in a manner similar to the unfolding patterns of ontogenesis from a single cell, that the conditions that occurred when amino acid formation and likely polypeptide production first occurred may have set the direction for all subsequent phylogenetic development. Consequently electromagnetic conditions similar to those inferred to have been present during abiogenesis may still be relatively potent modifiers of basic cell dynamics. Here we report the potentially oncostatic effects of this procedure.

Our hypothesis was that a very narrow range of weak intensity, appropriately temporally patterned magnetic fields applied intermittently during the nocturnal period should suppress chemically-induced tumorogenesis. Approximately 6 minutes of exposure once per hour were calculated to be sufficient for influencing cells but without the counterproductive effects of habituation that sometimes results from continuous exposure. We selected nocturnal exposures because they would be more relevant to potential applications to human patients when protracted exposures would be less restrictive (the patients would be sleeping) and because of our measurements of the intrinsic oncostatic effects of physiological levels of melatonin when the circulating values compensate following brief suppressions during nocturnal magnetic field exposures. The object of our study was to discern if nocturnal exposures to these weak but specifically patterned magnetic fields could elicit qualitatively conspicuous and robust suppression of malignancies.

Experimental Procedures

A total of 14, Wistar albino female rats, approximately 90 days of age at the beginning of the experiment were housed 3 to 4 rats per plastic cage. The housing arrangements are shown in **Figure 1**. This is the same equipment employed for previous studies involving treatment of experimental allergic encephalomyelitis [6] and for inducing nocturnal seizures in rats whose limbic

Figure 1 Coils employed to generate the amplitude-modulated 7 Hz magnetic fields.

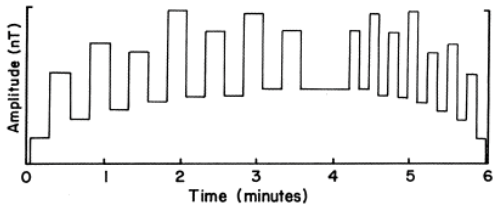

Figure 2 Shape of the 7 Hz Hz amplitude-modulated magnetic field to which the rats were exposed for 5 min and 50 s once per hour 8 times per night for one year.

epilepsy was induced by lithium and pilocarine [12]. By gavage, each rat received 1 cc of 2 mg of 7,11,Dimethylbenzl(a)anthracene (DMBA), a classical tumor-inducing agent, suspended in sesamie oil once per week for 4 weeks.

Immediately after the first injection the rats were exposed to one of four different average intensities of magnetic fields: 500 nT (upper left), 400 nT (upper right), 60 nT (lower left) and 30 nT (lower right) in **Figure 1.** The fields were generated through two Helmholtz coils whose characteristics have been reported [12]. Peripheral fields from these coils penetrated into the adjacent lower two plastic cages. We had established these "indirect" fields were effective and that the changes were not due to simply the position in previous experiments [6]. In other words if the field strengths in the coils were reduced by a factor of 10 to 50 nT, such that the intensities in the peripheral cages were less than 5 nT, there were no significant effects in the lower cages but only in the cages with 50 nT intensities.

This experimental arrangement was similar to the procedure we employed to reduce the severity of experimental allergic encephalomyelitis or EAE [7]. For one year, every night, a 7 Hz fundamental square wave created by a function generator was amplitude-modulated by a Commodore Computer 8 times per night (scotophase) between midnight and 0706 hr. The programmed photophase for the room was 12:12 with the dark onset occurring around 8 P.M. local time. A diagram of the escalating and deescalating amplitude modulated pattern is shown in **Figure 2.** The field pattern was activated for 5 min and

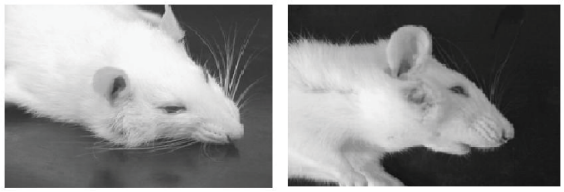

Figure 3 Salivatory tumor after about one year subsequent to the DMBA consumption.

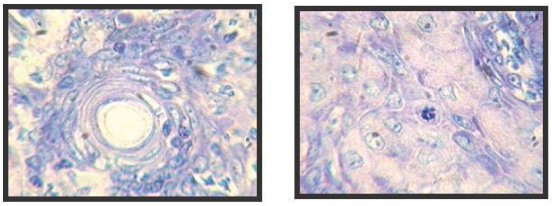

Figure 4 Histopathology of salivatory tumor from Figure 6. (1000×, oil) Toluidine Blue O.

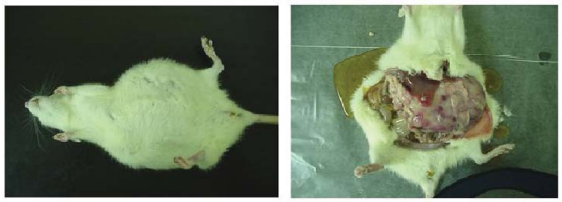

Figure 5 Pancreatic tumor about one year subsequent to DMBA consumption.

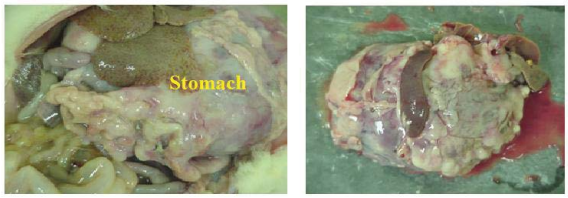

Figure 6 Organ depiction of tumor shown in Figure 5. The proliferation of anomalous tissue can be seen as the light yellowish-grey tissue wrapped around the abdominal mass.

50 s once per hour 8 times per night every night for one year. Food (Purina rat chow) and water were available ad libitum. The quarter-inch corn cob that served as bedding for the rats was removed and replaced once every two to three days before the onset of the scotophase.

Towards the end of the one year period, as various tumors became apparent for some exposure intensities, care was taken to ensure minimum distress for the rats. Approximately one year after the initial gavaging and the exposure to various intensity magnetic fields the rats were killed by barbiturate overdose. Necropsies were performed and appropriate pictures were taken. Sample tissue from the malignant growths were fixed in ethanol-formalin-acetic acid, processed, sectioned at 6 μ with a microtome, and stained with toluidine Blue O. The sections were examined by light microscopy between 40× and 1000×.

Results

The results were conspicuous. None of the 7 rats that had been administered the DMBA over four weeks and exposed to the 400 to 500 nT, nocturnal, intermittent amplitude-modulated 7 Hz fields developed any discernable tissue anomalies within the limits of visual inspection during necropsy. However 5 of the 7 rats that had been exposed to the same pattern of magnetic fields but with intensities between 30 to 60 nT developed conspicuous tumors peripherally. We had recorded and measured more than 300 rats of approximately 3,000 rats over a 25 year period that lived to clinical endpoints (two to three years of age). The vast majority of those tumors were mammary adenocarcinomas (verified by histology) or fibroadenomas. Two of the rats exposed to the 30 to 60 nT fields displayed this form. However there were additional types of tumors obtained with the DMBA treatments that we have not observed in our rat populations. The first type is shown for one rat in **Figure 3.** It was verified as a salivatory tumor (**Figure 4**).

The second type of tumor primarily involved the pancreas as shown in **Figure 5**. Despite the abdominal distention, this animal consumed food normally, acquired adipose, and exhibited no discernable indictors of distress. Even when given the option to consume Tylenol in solution or tap water in a two bottle choice paradigm, a procedure which has been shown to reflect nociception of the animal [13] and allows a rat to "titrate" its own "level of analgesia" the rat only consumed water. However the criteria for termination had been met because the rat was no longer eating and had become lethargic. The right picture reveals the mass responsible for the abdominal distention.

A closer inspection of the nodular mass within the viscera is

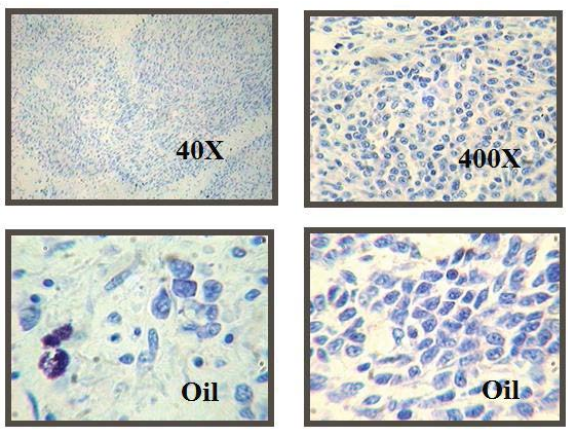

Figure 7 Histopathology at various levels of magnification (oil=1000×) within pancreatic malignant tissue shown in Figure 6.

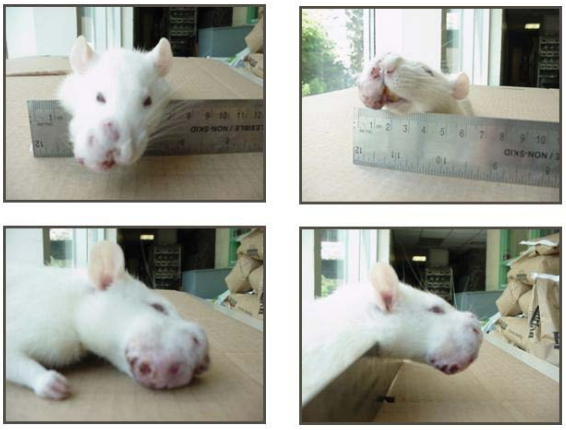

Figure 8 Gross display of nasal tumour that developed over one year in a rat that received the DBMA treatment.

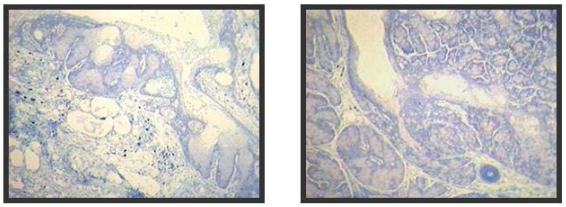

Figure 9 Histopathology of nasal tumor noted in Figure 10 (100×).

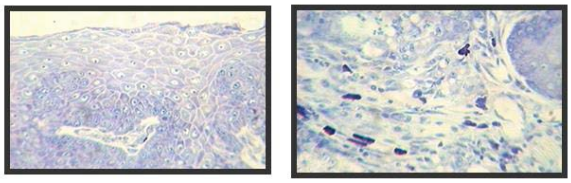

Figure 10 Histopathology of nasal tumor (400×). Hyaline cartilage is noted on left; mast cells (deep purple) infiltrating the connective tissue associated with the proliferation and external expansion of the tumor are evident on the right.

shown in **Figure 6** before (left) and after (right) removal from the animal. The absence of food components within the intestines is evident. **Figure 7** shows the histology. **Figure 8** through **Figure 10** demonstrate the gross characteristics and histology of the malignant growth within the nasal region of the rat.

Discussion

We have been investigating the effects of various teratogens and carcinogenic compounds for several decades. DMBA was selected because of its reliable induction of aberrant or malignant cells depending upon where within the body boundaries the material is administered. Most studies have pursued the proclivity for the enhancement of mammary tissues. In our experiments the material was delivered through the oral-digestive system. Consequently the occurrence of aberrant growths that slowly occurred over several months within the salivatory glands, nasal region (considering the likelihood that some rats may have aspired some of the substance through the Eustachian tube during gavaging) and the pancreas might be expected.

We had anticipated that the exposure to the same pattern and intensity of magnetic fields that attenuated experimental allergic encephalomyelitis would have been most beneficial. However for this particular treatment the 400 to 500 nT intensities of the 7 Hz amplitude modulated magnetic field were most effective. We have not observed such efficacy in any of our previous treatments for delaying or eliminating the growth of tumors. However in most of our studies the exposures have been much shorter, such as two or three weeks. Although the sample size might be considered too small from some perspectives, the qualitatively conspicuous tumors that occurred in one group (the low intensity field) compared to the display of no tumors in the group that was exposed at the same time but to higher intensity fields suggests this is a powerful effect. We cannot exclude the possibility that the marked group difference was a combination effect. Whereas the 400 to 500 nT suppressed malignant cell growth the lower intensities also increased this growth, thus enhancing the size of the effect.

Our approach has been that the solution for successful treatment of oncogenic processes requires the understanding of the biophysical mechanisms [14] at the level of quantum biology. Persinger [15] has shown quantitatively that a molarity-based Jacobson equation for relativistic resonance would be consistent with the effect upon a molecule with the mass of melatonin. The critical intensity would be about 10 to 100 nT. Nocturnal melatonin has been considered an oncostatic compound and its disruption could have occurred every night because of the multiple approximately 6 min, 7 Hz magnetic field exposures. It may be relevant that the 36 mHz and 71 mHz intrinsic periodicities for the shift in 7 Hz amplitudes (Figure 2) are also congruent with the resonance solution for calcium within the 15-20 nT range [15]. If these mechanisms operate in a manner similar to "narrow band" phenomena, then immediately adjacent bands ("intensities") might display enhanced refractory (protective) properties. Such a relationship would significantly challenge the classic linear approach to dosimetry for risk of malignant growth from carcinogenic stimuli.

The major limitation of this experiment was that prolonged time and investment were required to discern the oncostatic effects from the appropriate intensity of the magnetic field. However cancer often develops slowly, over decades, in the human being. Consequently preventive treatments for those prone to malignant cell growth might someday require life-long administration of the appropriately patterned and personalized magnetic field. If this procedure is effective for human conditions then the procedure could be applied without any invasiveness while the person sleeps. It would be analogous to preventing the opportunity for malaria to develop by sleeping in beds surrounded by mosquito nets to minimize its initiation by the critical vector.

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References

1. Wilson BW, Stevens RG, Andersen LE (1990) Extremely low frequency electromagnetic fields: the question of cancer. Battelle Press: Wash pp. 383.
2. Savitz DA, Wachtel H, Barnes FA, John EM, Tvrdik JG (1988) Case-control study of childhood cancer and exposure to 60-Hz magnetic fields. Am J Epidemiol 128: 21-38.
3. Whissell PM, Persinger MA (2007) Emerging synergisms between drugs and physiologically-patterned weak magnetic fields: implications for neuropharmacology and the human population in the twenty-first century. Cur Neuropharmacol 5: 278-288.
4. Thomas JR, Burch LS, Yeandle SS (1979) Microwave radiation and chlordiazepoxide: synergistic effects on fixed-interval behavior. Science 203: 1357-1358.
5. Mevissen M, Kietzmann M, Loescher W (1995) In vivo exposure of rats to a weak alternating magnetic field increases ornithine decarboxylase activity in mammary gland by a similar extent as the carcinogen DMBA. Cancer Lett 90: 207-214.
6. Cook LL, Persinger MA (2000) Suppression of experimental allergic encephalomyelitis is specific to the frequency and intensity of nocturnally applied, intermittent magnetic fields in rats. Neurosci Lett 292: 171-174.
7. Kinoshameg SA, Persinger MA (2004) Suppression of experimental allergic encephalomyelitis in rats by 50-nT, 7-Hz amplitude-modulated nocturnal magnetic fields depends on when after inoculation the fields are applied. Neurosci Lett 370: 166-170.
8. Frenkel K, Wei L, Wei H (1995) 7,12-dimethylbenz[a]anthracene induces oxidative DNA modification in vivo. Free Radic Biol Med 19: 373-380.
9. Wang L, Yi T, Zhang W, Pardoll DM, Yu H (2010) IL-17 enhances tumor development in carcinogen-induced skin cancer. Cancer Res 70: 10112-10120.
10. Cherry N (2002) Schumann resonances: a plausible biophysical mechanism for the human health effects of solar/geomagnetic activity. Nat Haz 26: 279-331.
11. Cole FE, Graf ER (1974) Precambrian ELF and abiogenesis. In: Persinger MA (ed)ELF and VLF electromagnetic field effects. Plenum: NY 243-274.
12. Persinger MA (1996) Enhancement of limbic seizures by nocturnal application of experimental magnetic fields that simulate the magnitude and morphology of increases in geomagnetic activity. Int J Neurosci 86: 271-280.
13. Persinger MA (2003) Rats' preferences for an analgesic compared to water: an alternative to "killing the rat so it does not suffer". Percept Mot Skills 96: 674-680.
14. Persinger MA, Lafrenie RM (2014) the cell plasma membrane potentials as energetic equivalents to astrophysical properties. Int. Lett. Chem Phys Astron 17: 67-77.
15. Persinger MA (2006) A potential multiple resonance mechanism by weak magnetic fields affect molecules and medical problems: the example of melatonin and experimental “multiple sclerosis”. Med Hypoth 66: 811-815.