http://www.ncbi.nlm.nih.gov/pubmed/8912234?

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### <u>J Pineal Res.</u> 1996 Sep;21(2):91-100.

# Effects of exposure to 16.7 Hz magnetic fields on urinary 6-hydroxymelatonin sulfate excretion of Swiss railway workers.

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The aim of our study was to examine the effects of 16.7 Hz electromagnetic-field exposure on pineal melatonin production in healthy humans. The study was based on comparing urinary 6hydroxymelatonin sulfate (6-OHMS) levels of 108 male railway workers between leisure periods and days following the start of service on electrically powered engines (66 engineers) or working beneath transmission lines (42 railway employees such as train attendants and station managers; controls). A repeated measures design was used, i.e., each volunteer served as his own control. The exposure averaged 20 muTesla in the most exposed workers and around 1 muTesla in the least exposed. Apart from magnetic exposure the workers were subject to a shift work schedule with daily advances between 15 min and 1 hr. Melatonin was assessed by sampling urinary 6-OHMS both in the morning and the early evening. Evening 6-OHMS values appeared to be lowered by a factor of 0.81 (95%CI: 0.73-0.90) during work days compared to leisure days among engine drivers, but not in the controls. The lowering was not confined to certain types of shift work such as early, normal, or late shifts. During subsequent leisure periods evening values recovered significantly, mean ratio = 1.27 (95%CI: 1.03-1.56), i.e., the effects appeared to be reversible. In contrast, morning 6-OHMS samples of engineers and controls did not differ much between work and leisure days. There was, however, a tendency for a rebound of morning values in a leisure period following a work period both for engineers and controls. The observed pattern appears to be in line with predictions of the "phase response curve." No evidence for a dose-response relation was found. The results support the hypothesis that 16.7 Hz magnetic fields alter 6-OHMS excretion in humans exposed to magnetic fields. An alternative explanation that cannot be excluded in this study is that the difference between engineers and controls is due to differential exposure to day light at work.

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Neurosci Lett. 2002 Nov 29;333(3):175-8.

## Responses of neurons to an amplitude modulated microwave stimulus.

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In this study we investigated the effects of a pulsed radio frequency signal similar to the signal produced by global system for mobile communication telephones (900 MHz carrier, modulated at 217 Hz) on neurons of the avian brain. We found that such stimulation resulted in changes in the amount of neural activity by more than half of the brain cells. Most (76%) of the responding cells increased their rates of firing by an average 3.5-fold. The other responding cells exhibited a decrease in their rates of spontaneous activity. Such responses indicate potential effects on humans using hand-held cellular phones.

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Bioelectromagnetics. 1988;9(2):195-205.

## Chronic exposure to ELF fields may induce depression.

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Exposure to extremely-low-frequency (ELF) electric or magnetic fields has been postulated as a potentially contributing factor in depression. Epidemiologic studies have yielded positive correlations between magnetic- and/or electric-field strengths in local environments and the incidence of depression-related suicide. Chronic exposure to ELF electric or magnetic fields can disrupt normal circadian rhythms in rat pineal serotonin-N-acetyltransferase activity as well as in serotonin and melatonin concentrations. Such disruptions in the circadian rhythmicity of pineal melatonin secretion have been associated with certain depressive disorders in human beings. In the rat, ELF fields may interfere with tonic aspects of neuronal input to the pineal gland, giving rise to what may be termed "functional pinealectomy." If long-term exposure to ELF fields causes pineal dysfunction in human beings as it does in the rat, such dysfunction may contribute to the onset of depression or may exacerbate existing depressive disorders.

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ordinalpos=173&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\_ResultsPanel.Pubmed\_DefaultRep ortPanel.Pubmed\_RVDocSum

Exp Brain Res. 1983;50(2-3):426-32.

# Effects of an artificial magnetic field on serotonin N-acetyltransferase activity and melatonin content of the rat pineal gland.

Welker HA, Semm P, Willig RP, Commentz JC, Wiltschko W, Vollrath L.

In the present study the effects of artificial magnetic fields on pineal serotonin-N-acetyltransferase (NAT) activity and melatonin content in male Sprague-Dawley rats were investigated to study the secretory activity of the pineal gland. Experimental inversion of the horizontal component of the natural magnetic field, performed at night-time, led to a significant decrease of both parameters investigated. During day-time, this effect was less conspicuous. During night-time, inversion of the horizontal component is followed by a reduced pineal secretory activity for about 2 h. After 24 h exposure to the inverted horizontal component, return to the natural condition was followed by a renewed clear depression of pineal NAT activity and melatonin content, indicating that the main stimulus is not the inverted magnetic field itself but rather its change. Changing the inclination of the local magnetic field from 63 degrees to 58 degrees, 68 degrees or 78 degrees, respectively also decreased the secretory activity of the rat pineal gland.

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<u>J Pineal Res.</u> 1990;9(4):259-69.

# Evidence for an effect of ELF electromagnetic fields on human pineal gland function.

<u>Wilson BW</u>, <u>Wright CW</u>, <u>Morris JE</u>, <u>Buschbom RL</u>, <u>Brown DP</u>, <u>Miller DL</u>, <u>Sommers-</u> <u>Flannigan R</u>, <u>Anderson LE</u>.

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A study was carried out to determine possible effects of 60-Hz electromagnetic-field exposure on pineal gland function in humans. Overnight excretion of urinary 6-hydroxymelatonin sulfate (6-OHMS), a stable urinary metabolite of the pineal hormone melatonin, was used to assess pineal gland function in 42 volunteers who used standard (conventional) or modified continuous polymer wire (CPW) electric blankets for approximately 8 weeks. Volunteers using conventional electric blankets showed no variations in 6-OHMS excretion as either a group or individuals during the study period. Serving as their own controls, 7 of 28 volunteers using the CPW blankets showed statistically significant changes in their mean nighttime 6-OHMS excretion. The CPW blankets switched on and off approximately twice as often when in service and produced magnetic fields that were 50% stronger than those from the conventional electric blankets. On the basis of these findings, we hypothesize that periodic exposure to pulsed DC or extremely low frequency electric or magnetic fields of sufficient intensity and duration can affect pineal gland function in certain individuals.

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FASEB J. 1992 Mar;6(6):2283-7.

# Magnetic field effects on pineal indoleamine metabolism and possible biological consequences.

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In recent years, there has been a great deal of publicity concerning the possible health effects of electric and/or magnetic field exposure. One of the most frequently reported observations after the exposure of animals to either electric or magnetic fields relates to alterations in the metabolism of serotonin (5HT) to melatonin within the pineal gland. This review summarizes these results particularly in animals exposed to intermittently inverted, non-time varying magnetic fields, i.e., pulsed static magnetic fields. When exposure occurs at night, the conversation of 5HT to melatonin is typically depressed, not unlike that after light exposure at night. The mechanisms by which pulsed magnetic fields alter the ability of the pineal to convert 5HT to the chief pineal hormone melatonin remains unknown but may involve effects on any or all of the following: the retinas, the suprachiasmatic nuclei, the peripheral sympathetic nervous system, and the pinealocytes. Results to date suggest that induced electrical currents (eddy currents) produced by the pulsed magnetic fields are particularly detrimental to pineal indoleamine metabolism and may be an important causative factor in the metabolic changes measured. The physiological consequences of perturbations in the melatonin rhythm induced by magnetic field exposure remain unknown.

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### Regul Toxicol Pharmacol. 1992 Jun;15(3):226-44.

# Alterations of the circadian melatonin rhythm by the electromagnetic spectrum: a study in environmental toxicology.

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The nightly production and secretion of melatonin by the pineal gland, an endocrine organ near the anatomical center of the brain, provides important time-of-day and time-of-year information to the remainder of the body. In mammals, the circadian rhythm of melatonin (low levels during the day and high levels at night) is synchronized by the prevailing light:dark environment with the retinas of the eyes doing the photoreception required for the induction of this rhythm. The advent of artificial light sources has allowed animals or humans to be exposed to light at unusual times, i.e., during the night. Light falling on the retinas at night leads to a rapid depression in the production and secretion of melatonin by the pineal gland. The magnitude of the drop in circulating melatonin due to light exposure at night is related to the brightness (intensity) as well as the wavelength (color) of light to which humans are exposed. The lowered melatonin values following unusual light exposure at night provide erroneous information to a number of organs that respond to the melatonin message since the signal implies it is day when, in fact, it is still night. Besides visible light, certain ultraviolet wavelengths as well as extremely low frequency electric and magnetic fields may also disturb the melatonin rhythm. These nonvisible wavelengths may influence the circadian melatonin rhythm by mechanisms similar to those by which light causes disturbances of melatonin production and release.

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Biomed Pharmacother. 1993;47(10):439-44.

## Electromagnetic fields and melatonin production.

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The pineal gland, which in humans is located near the anatomical center of the brain, is normally responsive to visible electromagnetic fields (ie light) since the eyes are functionally connected to the pineal gland by a series of neurons. Normally, the pineal gland produces low amounts of melatonin during the day and high amounts at night; this rhythm is reflected in the blood melatonin concentrations which are higher at night than during the day. In both man and lower mammals, their exposure to light at night is followed by a drop in pineal melatonin production and blood melatonin levels. Likewise, exposure of non-human mammals to sinusoidal electric and/or magnetic fields as well as pulsed static magnetic fields often reduces pineal melatonin production. Melatonin has many functions in the organism and any perturbation (not only electromagnetic fields) which causes levels of melatonin to be lower than normal may have significant physiological consequences. Melatonin, because it is a potent antioxidant, may provide significant protection against cancer initiation as well as promotion. However, it is premature to conclude that the alleged increased cancer risk reported in individuals living in higher than normal electromagnetic environments relate to reduced melatonin levels caused by such field exposures.

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#### <u>Rev Environ Health.</u> 1994 Jul-Dec;10(3-4):171-86.

# Melatonin suppression by static and extremely low frequency electromagnetic fields: relationship to the reported increased incidence of cancer.

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An increased cancer incidence has been reported in individuals living and/or working in an environment in which they are exposed to higher than normal artificial electromagnetic fields. One of the most uniform changes associated with the exposure of animals to either pulsed static geomagnetic fields or to sinusoidal extremely low frequency magnetic fields has been a reduction in high night-time levels of melatonin. Melatonin is a hormone produced especially at night in the pineal gland, a pea-sized organ near the center of the human brain. The high nocturnal production of melatonin leads to elevated blood melatonin levels at night as well. The exposure of humans or animals to light (visible electromagnetic radiation) at night rapidly depresses pineal melatonin production and blood melatonin levels. Likewise, the exposure of animals to various pulsed static and extremely low frequency magnetic fields also reduces melatonin levels. Melatonin is a potent oncostatic agent and it prevents both the initiation and promotion of cancer. Reduction of melatonin, at night, by any means, increases cells' vulnerability to alteration by carcinogenic agents. Thus, if in fact artificial electromagnetic field exposure increases the incidence of cancer in humans, a plausible mechanism could involve a reduction in melatonin which is the consequence of such exposures.

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#### <u>J Cell Biochem.</u> 2004 Sep 1;93(1):83-92.

# Extremely low frequency electromagnetic fields as effectors of cellular responses in vitro: possible immune cell activation.

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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.

### Bioelectromagnetics. 1990;11(4):349-58.

# Exposure of frog hearts to CW or amplitude-modulated VHF fields : selective efflux of calcium ions at 16 Hz.

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Isolated frog hearts were exposed for 30-min periods in a Crawford cell to a 240-MHz electromagnetic field, either continuous-wave or sinusoidally modulated at 0.5 or 16 Hz. Radiolabeled with calcium (45Ca), the hearts were observed for movement of Ca2+ at calculated SARs of 0.15, 0.24, 0.30, 0.36, 1.50, or 3.00 mW/kg. Neither CW radiation nor radiation at 0.5 Hz, which is close to the beating frequency of the frog's heart, affected movement of calcium ions. When the VHF field was modulated at 16 Hz, a field-intensity-dependent change in the efflux of calcium ions was observed. Relative to control values, ionic effluxes increased by about 18% at 0.3 mW/kg (P less than .01) and by 21% at 0.15 mW/kg (P less than .05), but movement of ions did not change significantly at other rates of energy deposition. These data indicate that the intact myocardium of the frog, akin to brain tissue of neonatal chicken, exhibits movement of calcium ions in response to a weak VHF field that is modulated at 16 Hz.

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