

1: J Orthop Res 2000 Jul;18(4):637-46

Pulsed electromagnetic field stimulation of MG63 osteoblast-like cells affects differentiation and local factor production.

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[Medline record in process]

Pulsed electromagnetic field stimulation has been used to promote the healing of chronic non-unions and fractures with delayed healing, but relatively little is known about its effects on osteogenic cells or the mechanisms involved. The purpose of this study was to examine the response of osteoblast-like cells to a pulsed electromagnetic field signal used clinically and to determine if the signal modulates the production of autocrine factors associated with differentiation. Confluent cultures of MG63 human osteoblast-like cells were placed between Helmholtz coils and exposed to a pulsed electromagnetic signal consisting of a burst of 20 pulses repeating at 15 Hz for 8 hours per day for 1, 2, or 4 days. Controls were cultured under identical conditions, but no signal was applied. Treated and control cultures were alternated between two comparable incubators and, therefore, between active coils; measurement of the temperature of the incubators and the culture medium indicated that application of the signal did not generate heat above the level found in the control incubator or culture medium. The pulsed electromagnetic signal caused a reduction in cell proliferation on the basis of cell number and [³H]thymidine incorporation. Cellular alkaline phosphatase-specific activity increased in the cultures exposed to the signal, with maximum effects at day 1. In contrast, enzyme activity in the cell-layer lysates, which included alkaline phosphatase-enriched extracellular matrix vesicles, continued to increase with the time of exposure to the signal. After 1 and 2 days of exposure, collagen synthesis and osteocalcin production were greater than in the control cultures. Prostaglandin E₂ in the treated cultures was significantly reduced at 1 and 2 days, whereas transforming growth factor-beta₁ was increased; at 4 days of treatment, however, the levels of both local factors were similar to those in the controls. The results indicate enhanced differentiation as the net effect of pulsed electromagnetic fields on osteoblasts, as evidenced by decreased proliferation and increased alkaline phosphatase-specific activity, osteocalcin synthesis, and collagen production. Pulsed electromagnetic field stimulation appears to promote the production of matrix vesicles on the basis of higher levels of alkaline phosphatase at 4 days in the cell layers than in the isolated cells, commensurate with osteogenic differentiation in response to transforming growth factor-beta₁. The results indicate that osteoblasts are sensitive to pulsed electromagnetic field stimulation, which alters cell activity through changes in local factor production.

PMID: 11052501, UI: 20505686

2: Adv Ther 2000 Mar-Apr;17(2):57-67

Spine fusion for discogenic low back pain: outcomes in patients treated with or without pulsed electromagnetic field stimulation.

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Sixty-one randomly selected patients who underwent lumbar fusion surgeries for

discogenic low back pain between 1987 and 1994 were retrospectively studied. All patients had failed to respond to preoperative conservative treatments. Forty-two patients received adjunctive therapy with pulsed electromagnetic field (PEMF) stimulation, and 19 patients received no electrical stimulation of any kind. Average follow-up time was 15.6 months postoperatively. Fusion succeeded in 97.6% of the PEMF group and in 52.6% of the unstimulated group ($P < .001$). The observed agreement between clinical and radiographic outcome was 75%. The use of PEMF stimulation enhances bony bridging in lumbar spinal fusions. Successful fusion underlies a good clinical outcome in patients with discogenic low back pain.

PMID: 11010056, UI: 20394475

3: Curr Rev Pain 1999;3(5):342-347

Sphenopalatine Ganglion Analgesia.

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[Record supplied by publisher]

The sphenopalatine ganglion and its involvement in the pathogenesis of pain has been the subject of debate for the last 90 years. The ganglion is a complex neural center composed of sensory, motor, and autonomic nerves, which makes it difficult to determine its pathophysiology. Current indications for blockade of the sphenopalatine ganglion include sphenopalatine and trigeminal neuralgia, migraine and cluster headaches, and atypical facial pain. Methods of blockade use local anesthetics, steroids, phenol, and conventional radiofrequency and electromagnetic field- pulsed radiofrequency lesioning. The techniques for blockade range from superficial to highly invasive. Efficacy studies, though few and small, show promise in patients who have failed pharmacologic or surgical therapies.

PMID: 10998690

4: J Nippon Med Sch 2000 Jun;67(3):198-201

A case of congenital pseudarthrosis of the tibia treated with pulsing electromagnetic fields. 17-year follow-up.

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Congenital pseudarthrosis of the tibia presents surgeons with one of the most challenging of all orthopedic problems. Various surgical treatments have succeeded only rarely. We report long-term follow-up of a patient with congenital pseudarthrosis of the tibia treated with pulsed electromagnetic fields (PEMF) and bone grafting. In this severe case, Bassett type III and Boyd type II, encouraging results were achieved with Boyd's dual onlay grafts and PEMF. Seven years after surgery, skeletal maturity was complete and an unacceptable degree of leg shortening had been avoided.

PMID: 10851354, UI: 20311526

5: Bioelectromagnetics 2000 May;21(4):272-86

Directed and enhanced neurite growth with pulsed magnetic field stimulation.

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Pulsed magnetic field (PMF) stimulation was applied to mammalian neurons in vitro to influence axonal growth and to determine whether induced current would direct and enhance neurite growth in the direction of the current. Two coils were constructed from individual sheets of copper folded into a square coil. Each coil was placed in a separate water-jacketed incubator. One was energized by a waveform generator driving a power amplifier, the other was not energized. Whole dorsal root ganglia (DRG) explant cultures from 15-day Sprague-Dawley rat embryos were established in supplemented media plus nerve growth factor (NGF) at concentrations of 0-100 ng/mL on a collagen-laminin substrate. Dishes were placed at the center of the top and bottom of both coils, so that the DRG were adjacent to the current flowing in the coil. After an initial 12 h allowing DRG attachment to the substrate floor, one coil was energized for 18 h, followed by a postexposure period of 18 h. Total incubation time was 48 h for all DRG cultures. At termination, DRG were histochemically stained for visualization and quantitative analysis of neurite outgrowth. Direction and length of neurite outgrowth were recorded with respect to direction of the current. PMF exposed DRG exhibited asymmetrical growth parallel to the current direction with concomitant enhancement of neurite length. DRG cultures not PMF exposed had a characteristic radial pattern of neurite outgrowth. These results suggest that PMF may offer a noninvasive mechanism to direct and promote nerve regeneration. Copyright 2000 Wiley-Liss, Inc.

PMID: 10797456, UI: 20259279

6: Bangladesh Med Res Counc Bull 1999 Apr;25(1):6-10

Pulsed electromagnetic fields for the treatment of bone fractures.

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The effectiveness of electrical stimulation and Pulsed Electro Magnetic Field (PEMF) stimulation for enhancement of bone healing has been reported by many workers. The mechanism of osteogenesis is not clear, therefore, studies look for empirical evidence. The present study involved a clinical trial using low amplitude PEMF on 19 patients with non-union or delayed union of the long bones. The pulse system used was similar in shape to Bassett's single pulse system where the electric voltage pulse was 0.3 mSec wide repeating every 12 mSec making a frequency of about 80 Hz. The peak magnetic fields were of the order of 0.01 to 0.1 m Tesla, hundred to thousand times smaller than that of Bassett. Among the 13 who completed this treatment schedule the history of non-union was an average of 41.3 weeks. Within an average treatment period of 14 weeks, 11 of the 13 patients had successful bone healing. The two unsuccessful cases had bone gaps greater than 1 cm following removal of dead bone after infection. However, use of such a low field negates Bassett's claim for a narrow window for shape and amplitude of wave form, and justifies further experimental study and an attempt to understand the underlying mechanism.

Publication Types:
Clinical trial

PMID: 10758655, UI: 20221825

7: J Spinal Cord Med 1999 Winter;22(4):239-45

The effect of pulsed electromagnetic fields on osteoporosis at the knee in individuals with spinal cord injury.

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The purpose of this study was to determine the effects of pulsed electromagnetic fields on osteoporotic bone at the knee in individuals with chronic spinal injury. The study consisted of 6 males with complete spinal cord injury at a minimum of 2 years duration. Bone mineral density (BMD) was obtained at both knees at initiation, 3 months, 6 months, and 12 months using dual energy X-ray absorptiometry. In each case, 1 knee was stimulated using The Bone Growth Stimulator Model 3005 from American Medical Electronics, Incorporated and the opposite knee served as the control. Stimulation ceased at 6 months. At 3 months BMD increased in the stimulated knees 5.1% and declined in the control knees 6.6% ($p < .05$ and $p < .02$, respectively). By 6 months the BMD returned to near baseline values and at 12 months both knees had lost bone at a similar rate to 2.4% below baseline for the stimulated knee and 3.6% below baseline for the control. There were larger effects closer to the site of stimulation. While the stimulation appeared useful in retarding osteoporosis, the unexpected exaggerated decline in the control knees and reversal at 6 months suggests underlying mechanisms are more complex than originally anticipated. The authors believe a local as well as a systemic response was created.

PMID: 10751127, UI: 20213179

8: Plast Reconstr Surg 2000 Apr;105(4):1371-4

Effects of pulsed magnetic energy on a microsurgically transferred vessel.

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This article reports the findings of a study that attempted to elucidate whether pulsed magnetic energy stimulates neovascularization in vivo, using a microsurgically created arterial loop model in a prospective randomized trial of 108 rats ($n = 12$ /group). Pulsed magnetic energies of 0.1 and 2.0 gauss were applied immediately postoperatively and for 4, 8, and 12 weeks, respectively, with a statistically significant increase in neovascularization among the treated animals compared with control rats. The study provides a starting point for future study and evaluation of the stimulation of angiogenesis with the use of pulsed magnetic energy and suggests a possible use of this modality to increase the quality of revascularized tissue.

PMID: 10744227, UI: 20206094

9: Cardiovasc Res 2000 Mar;45(4):1054-64

Elf-pulsed magnetic fields modulate opioid peptide gene expression in myocardial cells.

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OBJECTIVES: Magnetic fields have been shown to affect cell proliferation and growth factor expression in cultured cells. Although the activation of endorphin systems is a recurring motif among the biological events elicited by magnetic fields, compelling evidence indicating that magnetic fields may modulate opioid gene expression is still lacking. We therefore investigated whether extremely low frequency (ELF) pulsed magnetic fields (PMF) may affect opioid peptide gene expression and the signaling pathways controlling opioid peptide gene transcription in the adult ventricular myocyte, a cell type behaving both as a target and as a source for opioid peptides. **METHODS:** Prodynorphin gene expression was investigated in adult rat myocytes exposed to PMF by the aid of RNase protection and nuclear run-off transcription assays. In PMF-exposed nuclei, nuclear protein kinase C (PKC) activity was followed by measuring the phosphorylation rate of the acrylodan-labeled MARCKS peptide. The effect of PMF on the subcellular distribution of different PKC isozymes was assessed by immunoblotting. A radioimmunoassay procedure coupled to reversed-phase high performance liquid chromatography was used to monitor the expression of dynorphin B. **RESULTS:** Here, we show that PMF enhanced myocardial opioid gene expression and that a direct exposure of isolated myocyte nuclei to PMF markedly enhanced prodynorphin gene transcription, as in the intact cell. The PMF action was mediated by nuclear PKC activation but occurred independently from changes in PKC isozyme expression and enzyme translocation. PMF also led to a marked increase in the synthesis and secretion of dynorphin B. **CONCLUSIONS:** The present findings demonstrate that an opioid gene is activated by myocyte exposure to PMF and that the cell nucleus and nuclear embedded PKC are a crucial target for the PMF action. Due to the wide ranging importance of opioid peptides in myocardial cell homeostasis, the current data may suggest consideration for potential biological effects of PMF in the cardiovascular system.

PMID: 10728432, UI: 20192676

10: J Orthop Trauma 2000 Feb;14(2):93-100

Effects of pulsed electromagnetic fields on bone healing in a rabbit tibial osteotomy model.

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OBJECTIVE: The purpose of this study was to determine the effect of pulsed electromagnetic field (PEMF) exposure on healing tibial osteotomies in New Zealand White rabbits. **DESIGN:** One-millimeter Gigli saw osteotomies were stabilized by external fixation. One day after surgery, rabbits were randomly assigned to receive either no exposure (sham control) or thirty minutes or sixty minutes per day of low-frequency, low-amplitude PEMF. Radiographs were obtained weekly throughout the study. Rabbits were euthanized at fourteen, twenty-one, or twenty-eight days, and tibiae underwent either destructive torsional testing or histologic analysis. To determine the baseline torsional strength and stiffness of rabbit tibiae, eleven normal intact tibiae were tested to failure. **RESULTS:** Sixty-minute PEMF-treated osteotomies had significantly higher torsional strength than did sham controls at fourteen and twenty-one days postoperatively. Thirty-minute PEMF-treated osteotomies were significantly stronger than sham controls only after twenty-one days. Normal intact torsional strength was achieved by fourteen days in the sixty-minute PEMF group, by twenty-one days in the thirty-minute PEMF group, and by twenty-eight days in the sham controls. Maximum fracture callus area correlated with the time to reach normal torsional strength. **CONCLUSION:** In this animal model, low-frequency, low-amplitude PEMF significantly accelerated callus formation and osteotomy healing in a dose-dependent manner.

PMID: 10716379, UI: 20179123

11: Int J Neurosci 1999 Mar;97(1-2):139-45

Yawning and stretching induced by transcranial application of AC pulsed electromagnetic fields in Parkinson's disease.

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Yawning is considered a brainstem regulated behavior which is associated with changes in arousal and activity levels. Yawning and stretching are dopamine (DA) mediated behaviors and pharmacological studies indicate that these behaviors are associated with increased DA release coupled with stimulation of postsynaptic DA-D2 receptors. Despite their relation to the dopaminergic system, yawning and stretching are poorly documented in untreated or treated patients with Parkinson's disease (PD). A 49 year old fully medicated female patient with juvenile onset PD is presented in whom recurrent episodes of yawning and stretching developed during transcranial administration of AC pulsed electromagnetic fields (EMFs) of picotesla flux density. These episodes have not been observed previously in this or other patients during treatment with levodopa or DA receptor agonists or in unmedicated PD patients during treatment with AC pulsed EMFs. It is suggested that yawning and stretching behavior resulted in this patient from a synergistic interaction between EMFs and DA derived from levodopa supplementation with EMFs possibly facilitating the release of DA and simultaneously activating postsynaptic DA-D2 receptors in the nigrostriatal dopaminergic pathways. In addition, it is postulated that the release of ACTH/MSH peptides from peptidergic neurons in the brain upon stimulation of the DA-D2 receptors reinforced the yawning and stretching behavior.

PMID: 10681123, UI: 20143358

12: Rheum Dis Clin North Am 2000 Feb;26(1):51-62, viii

Electromagnetic fields and magnets. Investigational treatment for musculoskeletal disorders.

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Certain pulsed electromagnetic fields (PEMF) affect the growth of bone and cartilage in vitro, with potential application as an arthritis treatment. PEMF stimulation is already a proven remedy for delayed fractures, with potential clinical application for osteoarthritis, osteonecrosis of bone, osteoporosis, and wound healing. Static magnets may provide temporary pain relief under certain circumstances. In both cases, the available data is limited. The mechanisms underlying the use of PEMF and magnets are discussed.

Publication Types:

Review

Review, tutorial

PMID: 10680193, UI: 20144445

13: IEEE Eng Med Biol Mag 2000 Jan-Feb;19(1):131-7

Possible health hazards from exposure to power-frequency electric and magnetic fields--a COMAR Technical Information Statement.

In recent years concerns have been raised about the biological effects of exposure to electric and magnetic fields at extremely low frequencies (ELF), particularly those associated with the distribution and utilization of electric power. In 1989, the Institute of Electrical and Electronics Engineers (IEEE) issued an "Entity Position Statement" which stated that "there is not enough relevant scientific data to establish whether common exposure to power-frequency fields should be considered a health hazard" and that "there is general agreement that more research is needed to define safe limits of human exposure to power-frequency fields." After examination of relevant research reports published during the last ten years, COMAR concludes that it is highly unlikely that health problems can be associated with average 24-hour field exposure to power frequency magnetic fields of less than 1 microT (10 mG). Good laboratory evidence shows that magnetic fields 100 to 10,000 times higher than this level, either ELF sinusoidal or pulsed, can induce a variety of biological effects, including beneficial health effects such as bone or tissue healing. Many of the reports of effects of weaker fields should be considered preliminary, as some observations have not been reproduced in different laboratories, while others, observed in cells, have not been clearly connected to effects in intact animals. Also, the means of interaction of low-level ELF fields with cells, tissues or laboratory animals is not fully understood; therefore the health impacts of such weak fields on intact animals and humans, if any, cannot be predicted or explained. Further research is needed to confirm or negate reports of effects of weak fields, and to determine mechanisms and relevance of these effects to actual health hazards. Continued study in this complicated area will enhance our understanding of biological systems, as well as help identify levels and types of ELF exposure that may be deleterious to human health.

PMID: 10659440, UI: 20124665

14: Bioelectromagnetics 2000 Feb;21(2):112-21

Effects of PEMF on a murine osteosarcoma cell line: drug-resistant (P-glycoprotein-positive) and non-resistant cells.

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After pulsed exposure of Dunn osteosarcoma cells (nonresistant cells) to Adriamycin (ADR) at increasing concentrations and single-cell cloning of surviving cells, ADR-resistant cells were obtained. These resistant cells expressed P-glycoprotein and had resistance more than 10 times that of their nonresistant parent cells. Compared to the nonresistant cells not exposed to pulsing electromagnetic fields (PEMF) in ADR-free medium, their growth rates at ADR concentrations of 0.01 and 0.02 micrograms/ml, which were below IC50, were 83.0% and 61.8%, respectively. On the other hand, in the nonresistant cells exposed to PEMF (repetition frequency, 10 Hz; rise time, 25 microsec, peak magnetic field intensity, 0.4-0.8 mT), the growth rate was 111.9% in ADR-free medium, 95.5% at an ADR concentration of 0.01 micrograms/ml, and 92.2% at an ADR concentration of 0.02 micrograms/ml. This promotion of growth by PEMF is considered to be a result of mobilization of cells in the non-proliferative period of the cell cycle due to exposure to PEMF. However, at ADR concentrations above the IC50, the growth rate tended to decrease in the cells not exposed to PEMF. This may be caused by an increase in cells sensitive to ADR resulting from mobilization of cells in the non-proliferative period to the cell cycle. The

growth rate in the resistant cells exposed to PEMF was significantly lower than that in the non-exposed resistant cells at all ADR concentrations, including ADR-free culture ($P \leq 0.0114$). Therefore, this study suggests that PEMF promotes the growth of undifferentiated cells but progressively suppresses the growth of more differentiated cells, i.e., PEMF controls cell growth depending on the degree of cell differentiation. This study also shows the potentiality of PEMF as an adjunctive treatment method for malignant tumors. Copyright 2000 Wiley-Liss, Inc.

PMID: 10653622, UI: 20119138

15: Biochim Biophys Acta 2000 Jan 10;1495(1):90-111

Extremely low frequency pulsed DC electric fields promote neutrophil extension, metabolic resonance and DNA damage when phase-matched with metabolic oscillators.

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Application of extremely low frequency pulsed DC electric fields that are frequency- and phase-matched with endogenous metabolic oscillations leads to greatly exaggerated neutrophil extension and metabolic resonance wherein oscillatory NAD(P)H amplitudes are increased. In the presence of a resonant field, migrating cell length grows from 10 to approximately 40 microm, as does the overall length of microfilament assemblies. In contrast, cells stop locomotion and become spherical when exposed to phase-mismatched fields. Although cellular effects were not found to be dependent on electrode type and buffer, they were sensitive to temporal constraints (phase and pulse length) and cell surface charge. We suggest an electromechanical coupling hypothesis wherein applied electric fields and cytoskeletal polymerization forces act together to overcome the surface/cortical tension of neutrophils, thus promoting net cytoskeletal assembly and heightened metabolic amplitudes. Metabolic resonance enhances reactive oxygen metabolic production by neutrophils. Furthermore, cellular DNA damage was observed after prolonged metabolic resonance using both single cell gel electrophoresis ('comet' assay) and 3'-OH DNA labeling using terminal deoxynucleotidyl transferase. These results provide insights into transmembrane signal processing and cell interactions with weak electric fields.

PMID: 10634935, UI: 20102616

16: Bioelectromagnetics 2000 Jan;21(1):25-33

The use of nonlinear dielectric spectroscopy to monitor the bioelectromagnetic effects of a weak pulsed magnetic field in real time.

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Nonlinear dielectric spectroscopy (NLDS) was used to detect interaction of a pulsed magnetic field (PMF) with membrane protein dynamics in aggregating *Dictyostelium discoideum* amoebae. In the experiments reported here, a strong nonlinear dielectric response of *Dictyostelium discoideum* cells is shown, and a distinctive nonlinear dielectric response of cells previously exposed to PMF is shown. The method of NLDS is shown to be capable of monitoring and charting the

dynamic frequency response of the cell to an electromagnetic field. Copyright 2000 Wiley-Liss, Inc.

PMID: 10615089, UI: 20082763

17: Calcif Tissue Int 1999 Nov;65(5):396-401

Effects of pulsed electromagnetic fields on human chondrocytes: an in vitro study.

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(3)H-thymidine incorporation was studied in cultured human nasal and articular chondrocytes exposed to low-energy, low-frequency pulsed electromagnetic fields (PEMFs) (75 Hz, 2.3 mT). The reverse transcriptase polymerase chain reaction (RT-PCR) analysis shows that human secondary chondrocytes derived from both nasal and articular cartilage express collagen type II mRNA, which is a specific marker of the chondrocyte phenotype. In a preliminary series of experiments, cells were exposed to PEMF for different time periods ranging from 6 to 30 hours (time-course), in medium supplemented with 10% or 0.5% fetal calf serum (FCS) and in serum-free medium. The ratios between the (3)H-thymidine incorporation in PEMFs and control cultures show an increase of the cell proliferation in cultures exposed to PEMFs when serum is present in the culture medium, whereas no effect was observed in serum-free conditions. The increase in DNA synthesis, induced by PEMFs, was then evaluated only at the times of maximum induction and the results were analyzed by the three-factor analysis of variance (ANOVA). The data presented in this study show that even if (3)H-thymidine incorporation is higher in nasal than in articular chondrocytes, PEMF induce an increase in the proliferation of both cell types. Moreover, the concentration of FCS in the culture medium greatly influences the proliferative response of human chondrocytes to the PEMF exposure. Though normal human osteoblast cells increase their proliferation when exposed to PEMFs if only 10% FCS is present in the medium, human chondrocytes are able to increase their cell proliferation when exposed to PEMFs in the presence of both 0.5% and 10% of FCS in the medium. The results obtained may help to explain the basic mechanisms of PEMF stimulation of fracture healing.

PMID: 10541767, UI: 20009325

18: J Spinal Disord 1999 Oct;12(5):380-5

Effects of smoking and maturation on long-term maintenance of lumbar spinal fusion success.

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This is a follow-up study of a multicenter, randomized, placebo-controlled clinical trial conducted in accordance with the condition for Food and Drug Administration approval for pulsed electromagnetic fields. The purpose of this study was to evaluate the long-term efficacy and safety of pulsed electromagnetic fields for spinal fusion. An earlier clinical trial study was conducted to evaluate the efficacy of Pulsed Electromagnetic Fields to enhance fusion success at one year follow-up. In the original study, 195 patients undergoing interbody fusion were enrolled. Of the 195 patients, 98 were in the

active group and 97 were in the placebo group. Study results showed a 92% successful fusion rate in the active group compared to 68% in the placebo group. For this long-term follow-up study, all patients who had healed in the original study were recalled for a follow-up radiograph. Radiographs were assessed by the attending surgeon for fusion assessment, when possible. The results of this long-term follow-up study showed that there was a reduction in maintenance of the fusion over time by 25%, but that the reduction was unrelated to treatment group and correlated statistically with whether the patient was a smoker.

PMID: 10549700, UI: 20015893

19: Bioelectromagnetics 1999 Oct;20(7):453-8

**Published erratum appears in Bioelectromagnetics 2000 Jan;21(1):73
Power frequency fields promote cell differentiation coincident with an increase in transforming growth factor-beta(1) expression.**

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Recent information from several laboratories suggest that power frequency fields may stimulate cell differentiation in a number of model systems. In this way, they may be similar to pulsed electromagnetic fields, which have been used therapeutically. However, the effects of power frequency fields on phenotypic or genotypic expression have not been explained. This study describes the ability of power frequency fields to accelerate cell differentiation in vivo and describes dose relationships in terms of both amplitude and exposure duration. No change in proliferation or cell content were observed. A clear dose relationship, in terms of both amplitude and duration of exposure, was determined with the maximal biological response occurring at 0.1 mT and 7-9 h/day. Because this study was designed to explore biological activity at environmental exposure levels, this exposure range does not necessarily define optimal dosing conditions from the therapeutic point of view. This study reports the stimulation by power frequency fields of transforming growth factor-beta, an important signalling cytokine known to regulate cell differentiation. The hypothesis is raised that the stimulation of regulatory cytokines by electromagnetic fields may be an intermediary mechanism by which these fields have their biological activity.

PMID: 10495311, UI: 99425103

20: Int J Neurosci 1999 Aug;99(1-4):139-49

AC pulsed electromagnetic fields-induced sexual arousal and penile erections in Parkinson's disease.

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Sexual dysfunction is common in patients with Parkinson's disease (PD) since brain dopaminergic mechanisms are involved in the regulation of sexual behavior. Activation of dopamine D2 receptor sites, with resultant release of oxytocin from the paraventricular nucleus (PVN) of the hypothalamus, induces sexual arousal and erectile responses in experimental animals and humans. In Parkinsonian patients subcutaneous administration of apomorphine, a dopamine D2 receptor agonist, induces sexual arousal and penile erections. It has been

suggested that the therapeutic efficacy of transcranial administration of AC pulsed electromagnetic fields (EMFs) in the picotesla flux density in PD involves the activation of dopamine D2 receptor sites which are the principal site of action of dopaminergic pharmacotherapy in PD. Here, I report 2 elderly male PD patients who experienced sexual dysfunction which was recalcitrant to treatment with anti-Parkinsonian agents including selegiline, levodopa and tolcapone. However, brief transcranial administrations of AC pulsed EMFs in the picotesla flux density induced in these patients sexual arousal and spontaneous nocturnal erections. These findings support the notion that central activation of dopamine D2 receptor sites is associated with the therapeutic efficacy of AC pulsed EMFs in PD. In addition, since the right hemisphere is dominant for sexual activity, partly because of a dopaminergic bias of this hemisphere, these findings suggest that right hemispheric activation in response to administration of AC pulsed EMFs was associated in these patients with improved sexual functions.

PMID: 10495212, UI: 99423432

21: Int J Neurosci 1999 Apr;97(3-4):225-33

Treatment with AC pulsed electromagnetic fields improves olfactory function in Parkinson's disease.

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Olfactory dysfunction is a common symptom of Parkinson's disease (PD). It may manifest in the early stages of the disease and infrequently may even antedate the onset of motor symptoms. The cause of olfactory dysfunction in PD remains unknown. Pathological changes characteristic of PD (i.e., Lewy bodies) have been demonstrated in the olfactory bulb which contains a large population of dopaminergic neurons involved in olfactory information processing. Since dopaminergic drugs do not affect olfactory threshold in PD patients, it has been suggested that olfactory dysfunction in these patients is not dependent on dopamine deficiency. I present two fully medicated Parkinsonian patients with long standing history of olfactory dysfunction in whom recovery of smell occurred during therapeutic transcranial application of AC pulsed electromagnetic fields (EMFs) in the picotesla flux density. In both patients improvement of smell during administration of EMFs occurred in conjunction with recurrent episodes of yawning. The temporal association between recovery of smell and yawning behavior is remarkable since yawning is mediated by activation of a subpopulation of striatal and limbic postsynaptic dopamine D2 receptors induced by increased synaptic dopamine release. A high density of dopamine D2 receptors is present in the olfactory bulb and tract. Degeneration of olfactory dopaminergic neurons may lead to upregulation (i.e., supersensitivity) of postsynaptic dopamine D2 receptors. Presumably, small amounts of dopamine released into the synapses of the olfactory bulb during magnetic stimulation may cause activation of these supersensitive receptors resulting in enhanced sense of smell. Interestingly, in both patients enhancement of smell perception occurred only during administration of EMFs of 7 Hz frequency implying that the release of dopamine and activation of dopamine D2 receptors in the olfactory bulb was partly frequency dependent. In fact, weak magnetic fields have been found to cause interaction with biological systems only within narrow frequency ranges (i.e., frequency windows) and the existence of such frequency ranges has been explained on the basis of the cyclotron resonance model.

PMID: 10372649, UI: 99299864

22: Bioelectrochem Bioenerg 1999 Feb;48(1):149-62

A weak pulsed magnetic field affects adenine nucleotide oscillations, and related parameters in aggregating Dictyostelium discoideum amoebae.

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A model eukaryotic cell system was used to explore the effect of a weak pulsed magnetic field (PMF) on time-varying physiological parameters. Dictyostelium discoideum cells (V12 strain) were exposed to a pulsed magnetic field (PMF) of flux density 0.4 mT, generated via air-cored coils in trains of 2 ms pulses gated at 20 ms. This signal is similar to those used to treat non-uniting fractures. Samples were taken over periods of 20 min from harvested suspensions of amoebae during early aggregation phase, extracted and derivatised for HPLC fluorescent assay of adenine nucleotides. Analysis of variance showed a significant athermal damping effect ($P < 0.002$, $n = 22$) of the PMF on natural adenine nucleotide oscillations and some consistent changes in phase relationships. The technique of nonlinear dielectric spectroscopy (NLDS) revealed a distinctive effect of PMF, caffeine and EGTA in modulating the cellular harmonic response to an applied weak signal. Light scattering studies also showed altered frequency response of cells to PMF, EGTA and caffeine. PMF caused a significant reduction of caffeine induced cell contraction ($P < 0.0006$, $n = 19$ by paired t-test) as shown by Malvern particle size analyser, suggesting that intracellular calcium may be involved in mediating the effect of the PMF.

PMID: 10228582, UI: 99245266

23: Bioelectromagnetics 1999;20(3):177-82

Correlation between pulsed electromagnetic fields exposure time and cell proliferation increase in human osteosarcoma cell lines and human normal osteoblast cells in vitro.

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We have exposed cultured bone cells to a pulsed electromagnetic field (PEMF) for different times to find the minimal exposure time necessary to stimulate an increase of DNA synthesis. We used two different human osteosarcoma cell lines, TE-85 and MG-63, and human normal osteoblast cell (NHOC) obtained from surgical bone specimens. The cells were placed in multiwell plates and set in a tissue culture incubator between a pair of Helmholtz coils powered by a pulse generator (1.3-ms pulse, repeated at 75 Hz) for different periods of time. [³H]Thymidine incorporation was used to evaluate cell proliferation. The two osteosarcoma cell lines increase their thymidine incorporation when exposed to a PEMF for at least 30 min, both in a medium containing 10% fetal calf serum and in a serum-free medium. NHOC are known to increase their cell proliferation when exposed to PEMF but only if cultured in the presence of 10% fetal calf serum. In this experimental condition, three of the four cell lineages studied required at least 9 h of PEMF exposure to increase their DNA synthesis, whereas one cell lineage increased its cell proliferation after 6 h of PEMF exposure. Our observations confirm the hypothesis that the proliferative responses of NHOC and human osteosarcoma cell lines to PEMF exposure are quite different. Moreover, NHOC required minimal exposure times to PEMF to increase their cell proliferation, similar to that needed to stimulate bone formation in vivo.

PMID: 10194560, UI: 99210464

24: J Indian Med Assoc 1998 Sep;96(9):272-5

A study of the effects of pulsed electromagnetic field therapy with respect to serological grouping in rheumatoid arthritis.

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The positive role of pulsed electromagnetic field (PEMF) therapy in rheumatoid arthritis (RA) is known. The differential role of serological status of patients in RA is also well known. This paper presents a study of the differential effects of PEMF therapy on the two serological groups of patients. The responses of the seropositive patients are found to be more subdued. Varying effects of the therapy in alleviating the different symptomatology indicate that the rheumatoid factor (RF) is more resistant to PEMF.

PMID: 10063282, UI: 99162769

25: J Neurosci Res 1999 Jan 15;55(2):238-44

Effects of pulsed magnetic stimulation of GFAP levels in cultured astrocytes.

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The present study evaluates the physiological effects of magnetic stimulation on astrocyte cultures. Cell cultures were exposed to pulsed magnetic stimulation (10 Hz, 10 sec) at the following levels: 0.10 tesla (T; Group A); 0.21 T (Group B); 0.42 T (Group C); and 0.63 T (Group D). Glial fibrillary acidic protein (GFAP) levels from immunoblots, total protein concentrations, and cellular morphology were analyzed at 0, 1, 3, 5, 7, 13, and 20 days poststimulation. Significantly higher GFAP levels were observed in Group D at day 3 ($P = 0.0114$). The change was transient as the GFAP levels quickly returned to control levels by day 5. No other significant changes in GFAP levels were observed. In comparison to control protein levels at day 0, concentrations from Groups B, C, and D were significantly lower ($P < 0.006$), whereas at day 3, Groups C and D were significantly higher ($P < 0.02$). Differences in astrocyte morphology due to magnetic stimulation were not observed. This study demonstrated that high intensity magnetic stimulation for only 10 sec induced a transient biological response.

PMID: 9972826, UI: 99137111

26: J Neurosci Res 1999 Jan 15;55(2):230-7

Electromagnetic fields influence NGF activity and levels following sciatic nerve transection.

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Pulsed electromagnetic fields (PEMF) have been shown to increase the rate of nerve regeneration. Transient post-transection loss of target-derived nerve growth factor (NGF) is one mechanism proposed to signal induction of early nerve regenerative events. We tested the hypothesis that PEMF alter levels of NGF

activity and protein in injured nerve and/or dorsal root ganglia (DRG) during the first stages of regeneration (6-72 hr). Rats with a transection injury to the midhigh portion of the sciatic nerve on one side were exposed to PEMF or sham control PEMF for 4 hr/day for different time periods. NGF-like activity was determined in DRG, in 5-mm nerve segments proximal and distal to the transection site and in a corresponding 5-mm segment of the contralateral nonoperated nerve. NGF-like activity of coded tissue samples was measured in a blinded fashion using the chick DRG sensory neuron bioassay. Overall, PEMF caused a significant decrease in NGF-like activity in nerve tissue ($P < 0.02$, repeated measures analysis of variance, ANOVA) with decreases evident in proximal, distal, and contralateral nonoperated nerve. Unexpectedly, transection was also found to cause a significant ($P=0.001$) 2-fold increase in DRG NGF-like activity between 6 and 24 hr postinjury in contralateral but not ipsilateral DRG. PEMF also reduced NGF-like activity in DRG, although this decrease did not reach statistical significance. Assessment of the same nerve and DRG samples using ELISA and NGF-specific antibodies confirmed an overall significant ($P < 0.001$) decrease in NGF levels in PEMF-treated nerve tissue, while no decrease was detected in DRG or in nerve samples harvested from PEMF-treated uninjured rats. These findings demonstrate that PEMF can affect growth factor activity and levels, and raise the possibility that PEMF might promote nerve regeneration by amplifying the early postinjury decline in NGF activity.

PMID: 9972825, UI: 99137110

27: Eur J Ophthalmol 1998 Oct-Dec;8(4):253-7

The effect of pulsed electromagnetic field on patients with endocrine ophthalmopathy.

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PURPOSE: To evaluate eye signs, proptosis and ocular movements in patients with endocrine ophthalmopathy under the influence of pulsed electromagnetic field therapy. **METHODS:** We examined 14 patients (9 women, 5 men) with endocrine ophthalmopathy and evaluated eye signs, proptosis and ocular movements before and after the course of pulsed electromagnetic field therapy, and 12 controls. Their age ranged from 29 to 57 years. Visual sensitivity was investigated with a static automatic perimeter (Allergan Humphrey Field Analyzer). The score was calculated by rating the severity of involvement of soft tissue, proptosis, extraocular movements, corneal state and optic nerve function on a scale from 0 to 3. The pulsed electromagnetic field procedures were carried out with the help of electromagnetic spectacles. **RESULTS:** Pulsed electromagnetic field therapy reduced the score for soft tissue and proptosis in patients who suffered from endocrine ophthalmopathy. There was fall in the mean score for ocular movements, corneal and optic nerve function but it did not reach significance after treatment. Electromagnetic field therapy has no useful effect on visual signs and eye movements in two patients who had had the illness more than two years. **CONCLUSIONS:** Localised pulsed electromagnetic field procedures can be recommended, together with other methods of conservative treatment of endocrine ophthalmopathy.

PMID: 9891898, UI: 99109047

28: Bioelectromagnetics 1998;19(8):445-51

Pulsed electromagnetic fields enhance the induction of cytokines by peripheral blood mononuclear cells challenged with phytohemagglutinin.

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We evaluated the effects of a 50-Hz pulsed electromagnetic field on the production of cytokines by both resting and mitogen-treated peripheral blood mononuclear cells. Our results demonstrate that after exposure of normal cells to EMFs for 12 h, the levels of neither interleukin-1beta, nor interleukin-2 were increased. Indeed, the concentration of tumor necrosis factor alpha decreased significantly immediately after the exposure period. The results were, however, markedly different when cells were stimulated with phytohemagglutinin immediately before the exposure to EMFs. In this case the levels of cytokines, measured 24 and 48 h after the treatment, were 630 +/- 440 pg/ml and 910 +/- 530 pg/ml for interleukin-1beta, 530 +/- 330 pg/ml, and 860 +/- 560 pg/ml for tumor necrosis factor alpha, respectively. These values were significantly higher ($P < 0.05$) when compared with the controls. Interleukin-2 levels were significantly higher at the end of the EMF exposure only in supernatants of phytohemagglutinin-stimulated cells and, as a consequence of this increase, the proliferation indexes also were significantly increased 48 h after the EMFs' treatment. The comparison between biological activity and the cytokine antigen present in our samples indicated that the amount of antigen was paralleled by an equal recovery of biological activity. This suggests either the absence of qualitative differences in these proteins or the impairment of both the transcriptional and translational processes.

PMID: 9849913, UI: 99065165

29: Int J Neurosci 1998 Jul;95(1-2):107-13

Yawning and stretching--a behavioral syndrome associated with transcranial application of electromagnetic fields in multiple sclerosis.

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Intracerebral administration of adrenocorticotrophic hormone (ACTH) elicits in experimental animals a yawning stretching behavior which is believed to reflect an arousal response mediated through the septohippocampal cholinergic neurons. A surge in plasma ACTH levels at night and just prior to awakening from sleep is also associated in humans with yawning and stretching behavior. Recurrent episodes of uncontrollable yawning and body stretching, identical to those observed upon awakening from physiological sleep, occur in a subset of patients with multiple sclerosis (MS) during transcranial therapeutic application of AC pulsed electromagnetic fields of picotesla flux density. This behavioral response has been observed exclusively in young female patients who are fully ambulatory with a relapsing remitting course of the disease who also demonstrate a distinctly favorable therapeutic response to magnetic stimulation. ACTH is employed for the treatment of MS due to its immunomodulatory effects and a surge in its release in response to AC pulsed magnetic stimulation could explain some of the mechanism by which these fields improve symptoms of the disease.

Publication Types:

Review

Review, tutorial

PMID: 9845021, UI: 99059154

30: Neurosci Behav Physiol 1998 Sep-Oct;28(5):594-7

Magnetic and electrical stimulation in the rehabilitative treatment of patients with organic lesions of the nervous system.

Tyshkevich TG, Nikitina VV

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Studies were performed on 89 patients with organic lesions of the nervous system in which the leading clinical symptoms consisted of paralysis and pareses. Patients received complex treatment, including pulsed magnetic fields and an electrical stimulation regime producing multilevel stimulation. A control group of 49 patients with similar conditions was included, and these patients received only sinusoidal currents. Combined treatment with magnetic and electrical stimulation was more effective, as indicated by radiographic and electromyographic investigations.

Publication Types:
Clinical trial

PMID: 9809302, UI: 99026830

31: Int J Neurosci 1998 Sep;95(3-4):255-69

Reversal of the bicycle drawing direction in Parkinson's disease by AC pulsed electromagnetic fields.

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The Draw-a-Bicycle Test is employed in neuropsychological testing of cognitive skills since the bicycle design is widely known and also because of its complex structure. The Draw-a-Bicycle Test has been administered routinely to patients with Parkinson's disease (PD) and other neurodegenerative disorders to evaluate the effect of transcranial applications of AC pulsed electromagnetic fields (EMFs) in the picrotesla flux density on visuoconstructional skills. A seminal observation is reported in 5 medicated PD patients who demonstrated reversal of spontaneous drawing direction of the bicycle after they received a series of transcranial treatments with AC pulsed EMFs. In 3 patients reversal of the bicycle drawing direction was observed shortly after the administration of pulsed EMFs while in 2 patients these changes were observed within a time lag ranging from several weeks to months. All patients also demonstrated a dramatic clinical response to the administration of EMFs. These findings are intriguing because changes in drawing direction do not occur spontaneously in normal individuals as a result of relateralization of cognitive functions. This report suggests that administration of AC pulsed EMFs may induce in some PD patients changes in hemispheric dominance during processing of a visuoconstructional task and that these changes may be predictive of a particularly favourable response to AC pulsed EMFs therapy.

PMID: 9777443, UI: 98450618

32: Biochem Biophys Res Commun 1998 Sep 18;250(2):458-61

Pulsed electromagnetic fields simultaneously induce osteogenesis and upregulate transcription of bone morphogenetic proteins 2 and 4 in rat osteoblasts in vitro.

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Blake DR, Stevens CR

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Pulsed electromagnetic fields (PEMF) are successfully employed in the treatment of a variety of orthopaedic conditions, particularly delayed and nonunion fractures. In this study, we examined PEMF effects on in vitro osteogenesis by bone nodule formation and on mRNA expression of bone morphogenetic proteins 2 and 4 by reverse-transcriptase polymerase chain reaction (RT-PCR) in cultured rat calvarial osteoblasts. PEMF exposure induced a significant increase in both the number (39% over unexposed controls) and size (70% larger compared to unexposed controls) of bone-like nodules formed. PEMF also induced an increase in the levels of BMP-2 and BMP-4 mRNA in comparison to controls. This effect was directly related to the duration of PEMF exposure. This study shows that clinically applied PEMF have a reproducible osteogenic effect in vitro and simultaneously induce BMP-2 and -4 mRNA transcription. This supports the concept that the two effects are related.

PMID: 9753652, UI: 98440820

33: J Invest Dermatol 1998 Sep;111(3):457-63

A pulsed electric field enhances cutaneous delivery of methylene blue in excised full-thickness porcine skin.

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We used electric pulses to permeabilize porcine stratum corneum and demonstrate enhanced epidermal transport of methylene blue, a water-soluble cationic dye. Electrodes were placed on the outer surface of excised full-thickness porcine skin, and methylene blue was applied to the skin beneath the positive electrode; 1 ms pulses of up to 240 V were delivered at frequencies of 20-100 Hz for up to 30 min. The amount of dye in a skin sample was determined from absorbance spectra of dissolved punch biopsy sections. Penetration depth and concentration of the dye were measured with light and fluorescence microscopy of cryosections. At an electric exposure dose VT (applied voltage x frequency x pulse width x treatment duration) of about 4700 Vs, there is a threshold for efficient drug delivery. Increasing the applied voltage or field application time resulted in increased dye penetration. Transport induced by electric pulses was more than an order of magnitude greater than that seen following iontophoresis. We believe that the enhanced cutaneous delivery of methylene blue is due to a combination of de novo permeabilization of the stratum corneum by electric pulses, passive diffusion through the permeabilization sites, and electrophoretic and electroosmotic transport by the electric pulses. Pulsed electric fields may have important applications for drug delivery in a variety of fields where topical drug delivery is a goal.

PMID: 9740241, UI: 98410957

34: Am J Vet Res 1998 Sep;59(9):1177-81

Evaluation of treatment with a pulsed electromagnetic field on wound healing, clinicopathologic variables, and central nervous system activity of dogs.

Scardino MS, Swaim SF, Sartin EA, Steiss JE, Spano JS, Hoffman CE, Coolman SL,

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OBJECTIVE: To evaluate effects of treatment with a pulsed electromagnetic field (PEMF) on healing of open and sutured wounds, clinicopathologic variables, and CNS activity of dogs. **ANIMALS:** 12 adult female Beagles. **PROCEDURE:** Open and sutured wounds were created in the skin of the trunk of the dogs. Dogs were divided into 2 groups. One group received PEMF treatment and 1 group served as untreated (control) dogs. The PEMF-treated dogs received treatment twice a day starting the day before surgery and lasting through day 21 after surgery. Wounds were evaluated by use of tensiometry, planimetry, laser Doppler perfusion imaging, and histologic examination. Clinicopathologic variables and electroencephalographic tracings were also evaluated. **RESULTS:** Use of PEMF treatment resulted in significantly enhanced epithelialization of open wounds 10 and 15 days after surgery. Five days after surgery, wounds of control dogs had a negative value for wound contraction, whereas PEMF-treated wounds had a positive value. The PEMF treatment did not cause significant changes in short-term planimetric, perfusion, tensiometric, histologic, clinicopathologic, or electroencephalographic results. **CONCLUSIONS:** The PEMF treatment enhanced wound epithelialization in open cutaneous wounds and provided indications of early contraction without significant short-term changes in other variables.

PMID: 9736399, UI: 98405806

35: J Cell Physiol 1998 Sep;176(3):537-44

Effects of electromagnetic stimulation on the functional responsiveness of isolated rat osteoclasts.

Shankar VS, Simon BJ, Bax CM, Pazianas M, Moonga BS, Adebajo OA, Zaidi M

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We report the effects of pulsed electromagnetic fields (PEMFs) on the responsiveness of osteoclasts to cellular, hormonal, and ionic signals. Osteoclasts isolated from neonatal rat long bones were dispersed onto either slices of devitalised cortical bone (for the measurement of resorptive activity) or glass coverslips (for the determination of the cytosolic free Ca^{2+} concentration, $[\text{Ca}^{2+}]$). Osteoclasts were also cocultured on bone with osteoblastlike, UMR-106 cells. Bone resorption was quantitated by scanning electron microscopy and computer-assisted morphometry. PEMF application to osteoblast-osteoclast cocultures for 18 hr resulted in a twofold stimulation of bone resorption. In contrast, resorption by isolated osteoclasts remained unchanged in the presence of PEMFs, suggesting that osteoblasts were necessary for the PEMF-induced resorption stimulation seen in osteoblast-osteoclast cocultures. Furthermore, the potent inhibitory action of the hormone calcitonin on bone resorption was unaffected by PEMF application. However, PEMFs completely reversed another quite distinct action of calcitonin on the osteoclast: its potent inhibitory effect on the activation of the divalent cation-sensing (or Ca^{2+}) receptor. For these experiments, we made fura 2-based measurements of cytosolic $[\text{Ca}^{2+}]$ in single osteoclasts in response to the application of a known Ca^{2+} receptor agonist, Ni^{2+} . We first confirmed that activation of the osteoclast Ca^{2+} receptor by Ni^{2+} (5 mM) resulted in a characteristic monophasic elevation of cytosolic $[\text{Ca}^{2+}]$. As shown previously, this response was attenuated strongly by calcitonin at concentrations between 0.03 and 3 nM but remained intact in response to PEMFs. PEMF application, however, prevented the inhibitory effect of calcitonin on Ni^{2+} -induced cytosolic Ca^{2+} elevation. This suggested

that the fields disrupted the interaction between the calcitonin and Ca²⁺ receptor systems. In conclusion, we have shown that electromagnetic fields stimulate bone resorption through an action on the osteoblast and, by abolishing the inhibitory effects of calcitonin, also restore the responsiveness of osteoclasts to divalent cations.

PMID: 9699506, UI: 98363086

36: Bioelectromagnetics 1998;19(5):318-29

Inconsistent suppression of nocturnal pineal melatonin synthesis and serum melatonin levels in rats exposed to pulsed DC magnetic fields.

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The purpose of these experiments was to determine whether the exposure of rats at night to pulsed DC magnetic fields (MF) would influence the nocturnal production and secretion of melatonin, as indicated by pineal N-acetyltransferase (NAT) activity (the rate limiting enzyme in melatonin production) and pineal and serum melatonin levels. By using a computer-driven exposure system, 15 experiments were conducted. MF exposure onset was always during the night, with the duration of exposure varying from 15 to 120 min. A variety of field strengths, ranging from 50 to 500 microT (0.5 to 5.0 G) were used with the bulk of the studies being conducted using a 100 microT (1.0 G) field. During the interval of DC MF exposure, the field was turned on and off at 1-s intervals with a rise/fall time constant of 5 ms. Because the studies were performed during the night, all procedures were carried out under weak red light (intensity of <5 microW/cm²). At the conclusion of each study, a blood sample and the pineal gland were collected for analysis of serum melatonin titers and pineal NAT and melatonin levels. The outcome of individual studies varied. Of the 23 cases in which pineal NAT activity, pineal melatonin, and serum melatonin levels were measured, the following results were obtained; in 5 cases (21.7%) pineal NAT activity was depressed, in 2 cases (8.7%) studies pineal melatonin levels were lowered, and in 10 cases (43.5%) serum melatonin concentrations were reduced. Never was there a measured rise in any of the end points that were considered in this study. The magnitudes of the reductions were not correlated with field strength (i.e., no dose-response relationships were apparent), and likewise the reductions could not be correlated with the season of the year (experiments conducted at 12-month intervals under identical exposure conditions yielded different results). Duration of exposure also seemed not to be a factor in the degree of melatonin suppression. The inconsistency of the results does not permit the conclusion that pineal melatonin production or release are routinely influenced by pulsed DC MF exposure. In the current series of studies, a suppression of serum melatonin sometimes occurred in the absence of any apparent change in the synthesis of this indoleamine within the pineal gland (no alteration in either pineal NAT activity or pineal melatonin levels). Because melatonin is a direct free radical scavenger, the drop in serum melatonin could theoretically be explained by an increased uptake of melatonin by tissues that were experiencing augmented levels of free radicals as a consequence of MF exposure. This hypothetical possibly requires additional experimental documentation.

PMID: 9669546, UI: 98332209

37: Int J Neurosci 1998 Apr;93(3-4):239-50

Treatment with AC pulsed electromagnetic fields normalizes the latency of the

visual evoked response in a multiple sclerosis patient with optic atrophy.

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Visual evoked response (VER) studies have been utilized as supportive information for the diagnosis of multiple sclerosis (MS) and may be useful in objectively monitoring the effects of various therapeutic modalities. Delayed latency of the VER, which reflects slowed impulse transmission in the optic pathways, is the most characteristic abnormality associated with the disease. Brief transcranial applications of AC pulsed electromagnetic fields (EMFs) in the picotesla flux density are efficacious in the symptomatic treatment of MS and may also reestablish impulse transmission in the optic pathways. A 36 year old man developed an attack of right sided optic neuritis at the age of 30. On presentation he had blurring of vision with reduced acuity on the right and fundoscopic examination revealed pallor of the optic disc. A checkerboard pattern reversal VER showed a delayed latency to right eye stimulation (P100 = 132 ms; normal range: 95-115 ms). After he received two successive applications of AC pulsed EMFs of 7.5 picotesla flux density each of 20 minutes duration administered transcranially, there was a dramatic improvement in vision and the VER latency reverted to normal (P100= 107 ms). The rapid improvement in vision coupled with the normalization of the VER latency despite the presence of optic atrophy, which reflects chronic demyelination of the optic nerve, cannot be explained on the basis of partial or full reformation of myelin. It is proposed that in MS synaptic neurotransmitter deficiency is associated with the visual impairment and delayed VER latency following optic neuritis and that the recovery of the VER latency by treatment with pulsed EMFs is related to enhancement of synaptic neurotransmitter functions in the retina and central optic pathways. Recovery of the VER latency in MS patients may have important implications with respect to the treatment of visual impairment and prevention of visual loss. Specifically, repeated pulsed applications of EMFs may maintain impulse transmission in the optic nerve and thus potentially sustain its viability.

PMID: 9639241, UI: 98301112

38: Int J Neurosci 1998 May;94(1-2):41-54

Transcranial AC pulsed applications of weak electromagnetic fields reduces freezing and falling in progressive supranuclear palsy: a case report.

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Freezing is a common and disabling symptom in patients with Parkinsonism. It affects most commonly the gait in the form of start hesitation and sudden immobility often resulting in falling. A higher incidence of freezing occurs in patients with progressive supranuclear palsy (PSP) which is characterized clinically by a constellation of symptoms including supranuclear ophthalmoplegia, postural instability, axial rigidity, dysarthria, Parkinsonism, and pseudobulbar palsy. Pharmacologic therapy of PSP is currently disappointing and the disease progresses relentlessly to a fatal outcome within the first decade after onset. This report concerns a 67 year old woman with a diagnosis of PSP in whom freezing and frequent falling were the most disabling symptoms of the disease at the time of presentation. Both symptoms, which were rated 4 on the Unified Parkinson Rating Scale (UPRS) which grades Parkinsonian symptoms and

signs from 0 to 4, with 0 being normal and 4 being severe symptoms, were resistant to treatment with dopaminergic drugs such as levodopa, amantadine, selegiline and pergolide mesylate as well as with the potent and highly selective noradrenergic reuptake inhibitor nortriptyline. Weekly transcranial applications of AC pulsed electromagnetic fields (EMFs) of picotesla flux density was associated with approximately 50% reduction in the frequency of freezing and about 80-90% reduction in frequency of falling after a 6 months follow-up period. At this point freezing was rated 2 while falling received a score of 1 on the UPRS. In addition, this treatment was associated with an improvement in Parkinsonian and pseudobulbar symptoms with the difference between the pre-and post EMF treatment across 13 measures being highly significant ($p < .005$; Sign test). These results suggest that transcranial administration AC pulsed EMFs in the picotesla flux density is efficacious in the treatment of PSP.

PMID: 9622798, UI: 98286001

39: Int J Neurosci 1998 Feb;93(1-2):43-54

Reversal of a body image disorder (macrosomatognosia) in Parkinson's disease by treatment with AC pulsed electromagnetic fields.

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Macrosomatognosia refers to a disorder of the body image in which the patient perceives a part or parts of his body as disproportionately large. Macrosomatognosia has been associated with lesions in the parietal lobe, particularly the right parietal lobe, which integrates perceptual-sensorimotor functions concerned with the body image. It has been observed most commonly in patients with paroxysmal cerebral disorders such as epilepsy and migraine. The Draw-a-Person-Test has been employed in neuropsychological testing to identify disorders of the body image. Three fully medicated elderly Parkinsonian patients who exhibited, on the Draw-a-Person Test, macrosomatognosia involving the upper limbs are presented. In these patients spontaneous drawing of the figure of a man demonstrated disproportionately large arms. Furthermore, it was observed that the arm affected by tremor or, in the case of bilateral tremor, the arm showing the most severe tremor showed the greatest abnormality. This association implies that dopaminergic mechanisms influence neuronal systems in the nondominant right parietal lobe which construct the body image. After receiving a course of treatments with AC pulsed electromagnetic fields (EMFs) in the picotesla flux density applied transcranially, these patients' drawings showed reversal of the macrosomatognosia. These findings demonstrate that transcranial applications of AC pulsed EMFs affect the neuronal systems involved in the construction of the human body image and additionally reverse disorders of the body image in Parkinsonism which are related to right parietal lobe dysfunction.

PMID: 9604168, UI: 98267527

40: Arch Otolaryngol Head Neck Surg 1998 Apr;124(4):383-9

Effect of pulsed electromagnetic stimulation on facial nerve regeneration.

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OBJECTIVE: To determine if exposure to electromagnetic fields influences regeneration of the transected facial nerve in the rat. **DESIGN AND METHODS:** The left facial nerve was transected in the tympanic section of the fallopian canal in 24 rats randomly assigned to 2 groups. The cut ends of the facial nerve were reapproximated without sutures within the fallopian canal to maximize the potential for regeneration. Rats in the experimental group (n= 12) were then exposed to pulsed electromagnetic stimulation (0.4 millitesla at 120 Hz) for 4 hours per day, 5 days per week, for 8 weeks. Rats in the control group (n=12) were handled in an identical manner without pulsed electromagnetic stimulation. Four other rats were given sham operations in which all surgical procedures were carried out except for the actual nerve transection. Two of these rats were placed in each group. Nerve regeneration was evaluated using electroneurography (compound action potentials), force of whisker and eyelid movements, and voluntary facial movements before and at 2-week intervals after transection. Histological evaluation was performed at 10 weeks after transection. Each dependent variable was analyzed using a 2-way analysis of variance with 1 between variable (groups) and 1 within repeated measures variable (days after transection). **RESULTS:** Statistical analysis indicated that N1 (the negative deflection of depolarization phase of the muscle and/or nerve fibers) area, N1 amplitude, and N1 duration, as well as absolute amplitude of the compound action potentials, were all significantly greater 2 weeks after transection in the experimental than in the control group of rats. The force of eye and whisker movements after electrical stimulation was statistically greater in the experimental group of rats 4 weeks after transection. Voluntary eye movements in the experimental group were significantly better at 5 and 10 weeks, while whisker movements were better at 3 and 10 weeks. There was no statistical difference between the 2 groups for any histological variable. **CONCLUSION:** Results of this study indicate that pulsed electromagnetic stimulation enhances early regeneration of the transected facial nerve in rats.

PMID: 9559684, UI: 98218586

41: Orthopedics 1998 Mar;21(3):297-302

The effects of pulsed electromagnetism on fresh fracture healing: osteochondral repair in the rat femoral groove.

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Some clinical studies have claimed significant reductions in the healing time of fresh fractures with the use of pulsed electromagnetic fields (PEMFs). Animal models, however, have produced more equivocal results. This investigation examined the effects of PEMF treatment on an osteochondral defect placed in the patellofemoral groove of the rat. The results indicated that PEMF enhances early vascular reaction and suppresses initial pannus proliferation. Early chondrogenesis and bone formation were consistently stimulated, and the restoration of normal bone trabeculae advanced. Pulsed electromagnetic field treatment therefore may be useful in advancing repair during the early proliferative stage. Later results were variable and suggest that prolonged use may have deleterious effects, enhancing chondrogenesis beyond a point observed in normal repair and thus delaying normal subsurface trabeculation.

PMID: 9547814, UI: 98209034

42: Int J Neurosci 1997 Nov;92(1-2):95-102

Treatment with electromagnetic fields improves dual-task performance (talking

while walking) in multiple sclerosis.

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Multiple sclerosis (MS) is associated with an increased risk of falling resulting from visual disturbances, difficulties with gait and balance, apraxia of gait and peripheral neuropathy. These factors often interact synergistically to compromise the patient's gait stability. It has long been recognized that walking involves a cognitive component and that simultaneous cognitive and motor operations (dual-task) such as talking while walking may interfere with normal ambulation. Talking while walking reflects an example of a dual-task which is frequently impaired in MS patients. Impaired dual-task performance during walking may compromise the patient's gait and explain why in some circumstances, MS patients unexpectedly lose their balance and fall. Frontal lobe dysfunction, which commonly occurs in MS patients, may disrupt dual-task performance and increase the risk of falling in these patients. This report concerns a 36 old man with remitting-progressive MS with an EDSS score of 5.5 who experienced marked increase in spasticity in the legs and trunk and worsening of his gait and balance, occasionally resulting in falling, when talking while walking. His gait and balance improved dramatically after he received two successive transcranial treatments, each of 45 minutes, with AC pulsed electromagnetic fields (EMFs) of 7.5 picotesla flux density. Simultaneously, there was improvement in dual-task performance to the extent that talking while walking did not adversely affect his ambulation. In addition, neuropsychological testing revealed an almost 5-fold increase in word output on the Thurstone's Word-Fluency Test, which is sensitive to frontal lobe dysfunction. It is suggested that facilitation of dual-task performance during ambulation contributes to the overall improvement of gait and balance observed in MS patients receiving transcranial treatment with AC pulsed EMFs.

PMID: 9522259, UI: 98182728

43: Int J Neurosci 1997 Nov;92(1-2):63-72

Speech impairment in Parkinson's disease is improved by transcranial application of electromagnetic fields.

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A 52 year old fully medicated physician with juvenile onset Parkinsonism experienced 4 years ago severe "on-off" fluctuations in motor disability and debilitating speech impairment with severe stuttering which occurred predominantly during "on-off" periods. His speech impairment improved 20%-30% when sertraline (75 mg/day), a serotonin reuptake inhibitor, was added to his dopaminergic medications which included levodopa, amantadine, selegiline and pergolide mesylate. A more dramatic and consistent improvement in his speech occurred over the past 4 years during which time the patient received, on a fairly regular basis, weekly transcranial treatments with AC pulsed electromagnetic fields (EMFs) of picotesla flux density. Recurrence of speech impairment was observed on several occasions when regular treatments with EMFs were temporarily discontinued. These findings demonstrate that AC pulsed applications of picotesla flux density EMFs may offer a nonpharmacologic approach to the management of speech disturbances in Parkinsonism. Furthermore, this case implicates cerebral serotonergic deficiency in the pathogenesis of Parkinsonian speech impairment which affects more than 50% of patients. It is believed that pulsed applications of EMFs improved this patient's speech

impairment through the facilitation of serotonergic transmission which may have occurred in part through a synergistic interaction with sertraline.

PMID: 9522256, UI: 98182725

44: Radiat Res 1998 Mar;149(3):300-7

A test of lymphoma induction by long-term exposure of E mu-Pim1 transgenic mice to 50 Hz magnetic fields.

Harris AW, Basten A, Gebiski V, Noonan D, Finnie J, Bath ML, Bangay MJ, Repacholi MH

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E mu-Pim1 transgenic mice expressing a dysregulated Pim1 oncogene in their lymphoid cells were used to test whether exposure to 50 Hz magnetic fields can increase the frequency of malignant lymphoma in mice of a strain predisposed to develop such tumors spontaneously at low incidence. Specific-pathogen-free female mice were allocated randomly into groups of approximately 100 at 6-8 weeks of age and then exposed for 20 h/day for up to 18 months to sinusoidal magnetic fields of 0, 1, 100 or 1000 microT, or 1000 microT pulsed 15 min on and 15 min off. Additional E mu-Pim1 mice were injected with ethylnitrosourea (50 mg/kg body weight) as positive controls for enhanced lymphomagenesis; these yielded a cumulative incidence of lymphoma of 60% in 9 months. A lethal, transgene-dependent renal glomerular disease occurred at a frequency that varied from 9% to 19% among the groups, but the increase was statistically significant only at the 1000-microT exposure. Lymphoblastic and non-lymphoblastic (predominantly follicular) lymphomas were seen in 26 to 35% of the exposed mice, but at no significantly higher incidence than the 29% found in the sham-exposed mice. Hence we conclude that the lymphoma-prone mice did not reveal any tumorigenic effect of long-term exposure to 50 Hz magnetic fields.

PMID: 9496894, UI: 98156608

45: Int J Adult Orthodon Orthognath Surg 1997;12(1):43-53

Effects of static magnetic and pulsed electromagnetic fields on bone healing.

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The purpose of the present study was to evaluate the healing pattern of an experimentally induced osteotomy in Hartley guinea pigs in the presence of static magnetic and pulsed electromagnetic fields. The sample consisted of 30 Hartley guinea pigs 2 weeks of age divided into 3 groups: pulsed electromagnetic, static magnetic, and control. An osteotomy was performed in the mandibular postgonial area in all groups under general anesthesia. During the experimental period of 9 days, the animals were kept in experiment cages 8 hours per day, the first two groups being in the presence of pulsed electromagnetic and static magnetic field, respectively. Based on histologic results, both static and pulsed electromagnetic fields seemed to accelerate the rate of bone repair when compared to the control group. The osteotomy sites in the control animals consisted of connective tissue, while new bone had filled the osteotomy areas in both magnetic field groups.

PMID: 9456617, UI: 98117733

46: Bioelectromagnetics 1997;18(8):548-54

Short cycles of both static and pulsed electromagnetic fields have no effect on the induction of cytokines by peripheral blood mononuclear cells.

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We evaluated the effect of short cycles of static and pulsed electromagnetic field exposure on the eventual activation of peripheral blood mononuclear cells. The cells were subjected to three 15-min cycles of EMF, each exposure being followed by 105 min without a field, for a total of 6 hr. The results clearly demonstrate that the proliferative responses of both normal cells and cells stimulated with 1 microg/ml phytohemagglutinin were not distinguishable from control cells not exposed to EMF. Moreover, although the production of interleukin-2, interferon gamma and tumor necrosis factor alpha increased during the first 48 hr of incubation, the values remained unchanged with respect to controls. This indicates that brief exposure to an electromagnetic field has no significant effect on peripheral blood mononuclear cells. The comparison between biological activity and the cytokine antigen present in our samples indicated that the recovery of antigen corresponded to an equal recovery of biological activity, suggesting the absence of either qualitative differences in these proteins or the impairment of transcriptional and translational processes.

PMID: 9383243, UI: 98043591

47: Bioelectromagnetics 1997;18(8):541-7

Responses of human MG-63 osteosarcoma cell line and human osteoblast-like cells to pulsed electromagnetic fields.

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We have studied the effects of low-energy, low-frequency pulsed electromagnetic fields (PEMF) on cell proliferation, in both human osteoblast-like cells obtained from bone specimens and in human MG-63 osteosarcoma cell line. Assessment of osteoblastic phenotype was performed both by immunolabeling with antiosteonectin antibody and by verifying the presence of parathyroid hormone receptors. The cells were placed in multiwell plates and set in a tissue culture incubator between a pair of Helmholtz coils powered by a pulse generator (1.3 ms, 75 Hz) for different periods of time. [3H]Thymidine incorporation was used to evaluate cell proliferation. Since it had previously been observed that the osteoblast proliferative response to PEMF exposure may also be conditioned by the presence of serum in the medium, experiments were carried out at different serum concentrations. [3H]Thymidine incorporation increases in osteoblast-like cells, when they are exposed to PEMF in the presence of 10% fetal calf serum (FCS). The greatest effect is observed after 24 hours of PEMF exposure. No effects on cell proliferation are observed when osteoblast-like cells are exposed to PEMF in the presence of 0.5% FCS or in a serum-free medium. On the other hand, PEMF-exposed MG-63 cells show increased cell proliferation either at 10% FCS, 0.5% FCS and in serum-free medium. Nevertheless, the maximum effect of PEMF exposure on MG-63 cell proliferation depends on the percentage of FCS in the medium. The higher the FCS concentration, the faster the proliferative response to PEMF exposure. Our results show that, although MG-63 cells display some similarity with human bone cells, their responses to PEMF's exposure are quite different from that observed in normal human bone cells.

PMID: 9383242, UI: 98043590

48: Int J Neurosci 1997 Oct;91(3-4):189-97

Treatment with AC pulsed electromagnetic fields improves the response to levodopa in Parkinson's disease.

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A 52 year old fully medicated Parkinsonian patient with severe disability (stage 4 on the Hoehn & Yahr disability scale) became asymptomatic 10 weeks after he received twice weekly transcranial treatments with AC pulsed electromagnetic fields (EMFs) of picotesla flux density. Prior to treatment with EMFs, his medication (Sinemet CR) was about 50% effective and he experienced end-of-dose deterioration and diurnal-related decline in the drug's efficacy. For instance, while his morning medication was 90% effective, his afternoon medication was only 50% effective and his evening dose was only 30% effective. Ten weeks after introduction of treatment with EMFs, there was 40% improvement in his response to standard Sinemet medication with minimal change in its efficacy during the course of the day or evening. These findings demonstrate that intermittent, AC pulsed applications of picotesla flux density EMFs improve Parkinsonian symptoms in part by enhancing the patient's response to levodopa. This effect may be related to an increase in the capacity of striatal DA neurons to synthesize, store and release DA derived from exogenously supplied levodopa as well as to increased serotonin (5-HT) transmission which has been shown to enhance the response of PD patients to levodopa. Since decline in the response to levodopa is a phenomenon associated with progression of the disease, this case suggests that intermittent applications of AC pulsed EMFs of picotesla flux density reverse the course of chronic progressive PD.

PMID: 9394226, UI: 98056065

49: Int J Neurosci 1997 Sep;91(1-2):57-68

Reversal of cognitive impairment in an elderly parkinsonian patient by transcranial application of picotesla electromagnetic fields.

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A 74 year old retired building inspector with a 15 year history of Parkinson's disease (PD) presented with severe resting tremor in the right hand, generalized bradykinesia, difficulties with the initiation of gait with freezing, mental depression and generalized cognitive impairment despite being fully medicated. Testing of constructional abilities employing various drawing tasks demonstrated drawing impairment compatible with severe left hemispheric dysfunction. After receiving two successive transcranial applications, each of 20 minutes duration, with AC pulsed electromagnetic fields (EMFs) of 7.5 picotesla flux density and frequencies of 5Hz and 7Hz respectively, his tremor remitted and there was dramatic improvement in his drawing performance. Additional striking improvements in his drawing performance occurred over the following two days after he continued to receive daily treatments with EMFs. The patient's drawings were subjected to a Reliability Test in which 10 raters reported 100% correct assessment of pre- and post drawings with all possible comparisons (mean 2 = 5.0; $p < .05$). This case demonstrates in PD rapid reversal of drawing impairment related to left hemispheric dysfunction by brief transcranial applications of AC

pulsed picotesla flux density EMFs and suggests that cognitive deficits associated with Parkinsonism, which usually are progressive and unaffected by dopamine replacement therapy, may be partly reversed by administration of these EMFs. Treatment with picotesla EMFs reflects a "cutting edge" approach to the management of cognitive impairment in Parkinsonism.

PMID: 9394215, UI: 98056054

50: Indian J Lepr 1997 Jul-Sep;69(3):241-50

Exposure to pulsed magnetic fields in the treatment of plantar ulcers in leprosy patients--a pilot, randomized, double-blind, controlled clinical trial.

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A pilot, randomized, double-blind, controlled clinical trial to study the effect of exposure to pulsed magnetic fields (PMF) on the rate of healing of plantar ulcers in leprosy patients was undertaken. Twenty patients were randomly allocated to receive standard wound-care treatment (controls) and 20 others received standard treatment plus exposure to PMF (sinusoidal form, 0.95 to 1.05 Hz, amplitude +/- 2400 nano Teslas) (study group) for four weeks. Assessment of the outcome of treatment was based on the volume of ulcers, calculated from the maximal length, breadth and depth of the ulcer recorded on the day of admission, at one and two weeks and at the end of treatment. The analysis of the results was based on 15 control patients and 18 PMF patients after deletion of four patients due to irregularity in attendance and three others on account of suspected malignancy of the ulcers. In the control group, the geometric mean volumes of the ulcers were 2843 and 1478 cu mm on the day of admission and at the end of the treatment ($P = 0.03$); the corresponding values in the PMF group were 2428 and 337 cu mm, respectively ($P < 0.001$). A decrease in the volume of 40% or more was observed in 53% of control patients and 89% of PMF patients ($P = 0.02$); a decrease of 80% or more was observed in none of the controls and in 33% of PMF patients. These findings strongly suggest that exposure to PMF causes a significantly more rapid healing of plantar ulcers in leprosy patients.

Publication Types:

Clinical trial

Randomized controlled trial

PMID: 9394172, UI: 98056011