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Formulation of ELF magnetic fields' effects on malondialdehyde level and myeloperoxidase activity in kidney using genetic programming

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ABSTRACT

In vivo exposure effects of electromagnetic fields (EMFs) on various tissues of experiment animals have been investigated. In this sense, modeling and formulation of these biological effects have been of significant importance. In this study extremely low frequency (ELF) EMFs effects on malondialdehyde (MDA) level and myeloperoxidase (MPO) activity in kidney of guinea pigs exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT have been presented. It has been planned to determine whether genetic programming (GP) is appropriate to analyze and formulate these biological effects. Consequently, it has been observed that GP can be effectively used to model MDA level and MPO activity. The performances of prediction of the proposed GP formulation versus actual experimental values are found to be quite satisfactory in terms of standard deviation and correlation coefficient. It is concluded that the GP application serves to form a database for the researchers in this field, without exposing tissues to EMF and without using too many guinea pigs.

1. Introduction

Recently, the concerns of people about the possible effects of the electromagnetic fields (EMFs) on their health have been heightened with the increasing distribution and utilization of power frequency electric currents. For this reason, most scientists have focused on the effects of extremely low frequency (ELF; $f < 300$ Hz) EMF exposure on people's health and they have conducted several epidemiological and laboratory studies to define the risks of EMF exposures. There is a link between ELF magnetic field exposure and the increased incidence of certain types of tumor, particularly in leukemia and brain cancer [1–5]. The ELF EMF has been classified as 2B, possibly carcinogenic to humans, by the International Agency for Research on Cancer [5]. EMF exposure could affect gene expression, signal transduction, DNA damage and enzyme regulation [6–13].

Reactive oxygen species (ROS) are constantly generated in small amounts during metabolic processes. Recent studies have demonstrated that EMFs can cause increase in ROS formation and resulting oxidative stress [14–25]. Magnetic fields penetrate the cells and can alter cell membrane potential and the concentration of ions [26–28]. These alterations may affect free radical processes within the cell. Free radical formation induces changes in enzymes activity, gene expression, alteration of membrane structure and DNA damage [29]. The ELF EMF has been thought to prolong the life of free radicals and can act as a promoter or co-promoter of cancer [7]. Increased free radical activity in cellular levels can cause

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Table 1 – MPO activities and MDA levels in kidney tissues of exposed and control animals (mean ± S.E.M.)

Groups	n	MPO activity (U/g tissue)	n	MDA level (nmol/g tissue)
Control	8	0.636 ± 0.085	7	77.35 ± 6.54
1 mT; 4 h	7	0.928 ± 0.023*	8	104.53 ± 8.32*
1 mT; 8 h	7	0.815 ± 0.045	8	75.36 ± 4.00
2 mT; 4 h	6	0.914 ± 0.045*	6	160.00 ± 20.66*
2 mT; 8 h	7	1.054 ± 0.051*	7	68.75 ± 2.40
3 mT; 4 h	7	0.876 ± 0.050*	8	67.20 ± 7.03
3 mT; 8 h	7	0.927 ± 0.088	9	78.79 ± 5.61

* $p < 0.05$ with respect to controls.

increase in lipid peroxidation. Malondialdehyde (MDA) is the last product of lipid peroxidation [19,20]. On the other hand Myeloperoxidase (MPO—EC 1.11.1.7) is a bactericidal enzyme secreted by activated phagocytes that constitute the defense system of immune cells, specifically catalyzes the production of hypochlorous acid (HOCl) from chloride and hydrogen peroxide [10–12,30,31].

This study focuses on the modeling and formulation of the ELF magnetic fields' effects on MDA level and MPO activity in kidney using genetic programming (GP) based on experimental values. GP proposed by Koza [32] is an optimization technique which is a branch of genetic algorithms based on the principles of genetics and natural selection. In the application of GP, it has been verified that GP can be effectively used to model complex relationships especially where no valid models exist as in the case of MDA level and MPO activity considered in this study.

The paper is organized as follows: in the following section, it will be presented materials and methods, and biochemical results. In Section 3, summary of genetic programming; overview of gene expression programming (GEP) and solving a simple problem with GEP are given. Genetic programming is applied to experimental data in Section 4. The explicit formulation of GEP model for MPO level and MDA activity, and their results are discussed in Section 5. In the last section, the conclusions are expressed.

2. Materials and methods

The experimental protocol was reviewed and approved by the Laboratory Animal Care Committee of Gazi University (Report no.: 36-7838).

A total of 54 male, 250–300 g weighted (10–12 weeks aged) guinea pigs were used. The magnetic field exposure system was chosen as circular Helmholtz coils which were developed in Bioelectromagnetics Laboratory [33]. Coil pairs of Helmholtz configuration were used in the vertical manner. Animals were housed pairly in 26 cm × 22 cm × 10 cm plastic cages positioned at the center of the energized Helmholtz coil during experiments, to avoid any distortion of the generated magnetic fields. Forty-six guinea pigs were exposed to 50 Hz, 1 mT, 2 mT and 3 mT fields with the exposure periods of 4 h/day and 8 h/day for 5 days. Eight subjects were handled in an identical manner with the exposed animals in the same laboratory. They were housed at the center of the Helmholtz coils without being exposed to any magnetic fields and used as control. The animals were fed standard pellet food and kept in the laboratory at a room temperature of 23 ± 0.2 °C, a day and night cycle of 12 h and ambient geomagnetic field of 30 μT. To control possible variation in responses due to circadian rhythm, daily exposure periods of 4 h and 8 h were chosen between 8:00 to 12:00 a.m. and 8:00 a.m. to 4:00 p.m., respectively. After exposure periods, animals were sacrificed by ether inhalation in a closed box, and then kidneys were dissected out immediately. They shocked by liquid nitrogen and stored in deepfreeze at −40 °C until performing the analysis of MDA contents and at −70 °C until performing the analysis of MPO activity. MDA levels of renal tissues were determined according to the Cassini et al.'s spectrophotometric method [19,20,34]. MPO activity was assessed by measuring the H_2O_2-dependent oxidation of *o*-dianisidin. One unit (U) of enzyme activity was defined as the amount of MPO present that caused a change in absorbance of 1.0 min^{-1} at 410 nm and 37 °C [10–12,35].

Statistical analyses were carried out using SPSS software (SPSS 11.5 for windows, SPSS Inc., Chicago, USA). Comparisons between exposed groups and controls were made by using Mann Whitney *U*-test. The p value was considered significant at $p < 0.05$.

2.1. Biochemical results

MDA levels and MPO activities in kidney of guinea pigs exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT with the daily exposure periods of 4 h and 8 h for 5 days are given in Table 1 for mean ± standard error of means (S.E.M.) and statistics of experiment groups.

Statistically significant increases in kidney MDA levels were found for the magnetic fields of 1 mT and 2 mT with the daily exposure of 4 h [20]. Increased MPO activities in kidney of guinea pigs were also determined for all exposure groups with respect to controls except for the magnetic fields of 1 mT and 3 mT with the daily exposure of 8 h [10–12].

3. Summary of genetic programming

Genetic programming (GP) proposed by Koza [32] is an extension to genetic algorithms (GA). Koza defines GP as a domain-independent problem-solving approach in which computer programs are evolved to solve, or approximately solve, problems based on the Darwinian principle of reproduction and survival of the fittest and analogs of naturally occurring genetic operations such as crossover (sexual recombination) and mutation.