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A hypothetical mathematical construct explaining the mechanism of biological amplification in an experimental model utilizing picoTesla (PT) electromagnetic fields

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Summary We seek to answer the conundrum: What is the fundamental mechanism by which very weak, low frequency Electromagnetic fields influence biosystems? In considering the hydrophobicity of intramembranous protein (IMP) H-bonds which cross the phospholipid bilayer of plasma membranes, and the necessity for photonic recycling in cell surface interactions after dissipation of energetic states, present models lack structure and thermodynamic properties to maintain (ΔE) sufficient energy sources necessary for amplifications by factors of 10^{12}. Even though one accepts that the ligand–receptor association alters the conformation of extracellular, extruding portions of IMP's at the cell surface, and that this change can be transmitted to the cytoplasm by the transmembranous helical segments by nonlinear vibrations of proteins with generation of soliton waves, one is still unable to account for repair and balanced function. Indeed, responses of critical molecules to certain magnetic field signals may include enhanced vibrational amplitudes, increased quanta of thermal energies and order inducing interactions.

We may accept that microtrabecular reticulum-receptor is associated with actin filaments and ATP molecules which contribute to the activation of the cyclase enzyme system through piezoelectricity. Magnetic fields will pass through the membrane which sharply attenuates the electric field component of an EM field, due to its high impedance. Furthermore, EM oscillations are converted to mechanical vibrations; i.e., photon–phonon transduction, to induce molecular vibrations of frequencies specifically responsible for bioamplifications of weak triggers at the membrane surface, as well as GAP junctions. The hydrogen bonds of considerable importance are those in proteins (10^{12} Hz) and DNA (10^{11} Hz) and may be viewed as centers of EM radiation emission in the range from the mm microwaves to the far IR. However, classical electrodynamical theory does not yield a model for

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biomolecular resonant responses which are integrated over time and account for the connection between the phonon field and photons. Jacobson Resonance does supply an initial physical mechanism, as equivalencies in energy to that of Zeeman Resonance (i.e., zero-order magnetic resonance) and cyclotron resonance may be derived from the DeBroglie wave particle equation. For the first time, we view the introduction of Relativity Theory to biology in the expression,

$$mc^2 = BvLq,$$

where m is the mass of a particle in the 'box' or 'string' (molecule in a biosystem), c is the velocity of electromagnetic field in space, independent of its inertial frame of reference, B is the magnetic flux density, v is the velocity of the carrier or 'string' (a one or two dimensional 'box') in which the particle exists, L is its dimension (length) and q represents a unit charge $q = 1$ C, by defining electromotive force as energy per unit charge.

Equivalencies suggest that $qvBL$ is one of the fundamental expressions of energy of a charged wave-particle in magnetic fields, just as Zeeman and cyclotron resonance energy expressions, $g\beta B$ and $qhB/2\pi m$, and is applicable to all charged particles (molecules in biological systems). There may exist spontaneous, independent and incessant interactions of magnetic vector B and particles in biosystems which exert Lorentz forces. Lorentz forces may be transmitted from EM field to gravitational field as a gravity wave which return to the phonon field as microgravitational fluctuations to therein produce quantum vibrational states that increase quanta of thermal energies integrated over time. This may account for the differential of 10^{12} between photonic energy of ELF waves and the Boltzman energy kT.

Recent data from *in vivo* controlled studies are included as empirical support for the various hypotheses presented.

INTRODUCTION

Entropy (S) represents a property of a system that changes, when the system undergoes a reversible change, by an amount equal to the energy absorbed by the system. Entropy depends upon the state of the system, and it is a quantity with an arbitrary zero, with only changes in its value being of significance. The concept of entropy follows from the second law of thermodynamics as it applies to, for example, a reversible cycle wherein there is zero entropy change. For an irreversible process in an isolated system the entropy always increases. A biological system may be viewed, in some sense, as a closed circuit, e.g., B. Nordenstrom's system of biologically closed electric circuits (1,2), and changes are, to some extent, irreversible; and any spontaneous change occurring in a closed system is accompanied by an increase in entropy. The absolute value of the entropy of a system is a measure of the unavailability of its energy. A solid that is not perfect has a certain amount of disorder which leads to it possessing a configurational entropy.

In general, entropy can be thought of as a measure of the disorder of a system. In consideration of the subtle discontinuities and incoherences inherent in any system, including a biological system which in many respects may be viewed as the most ordered state of matter, there is nevertheless configurational entropy inherent in the vital structures such as proteins which reduce ΔE, the free energy of a system available for ordering production of ATP which drives the metabolic engine of life. When there are configurational entropies, congruence of oscillatory trajectories of biological microcomponents is diminished as well as coherence and confluence of the molecules of the solvent, i.e., water molecules. Biophotonic emissions from hydrogen bonds incessantly may adjust coherence and correlate spin angular momenta of baryons and leptons, thus regulating particle jumps and the level of entropy while adjusting availability of energy for driving biological processes. While transductive coupling of signals across the plasma membrane is enhanced by an increase in ΔE available from within the cell, and the preparation of coherent charged states of cell surface receptors are responsible for the wave of excitation and dissipation of energy rolling across the cellular membranes in dissipative reactions controlling calcium uptake and efflux, there must be a fundamental initiating physical phenomenon inexplicable with classical electro-dynamical theory which accounts for decrease in entropy and greater utilization and production of free energy. This fundamental mechanism is speculated to be based in biomolecular resonance, a discrete interaction based upon in-phase vibrations setting conditions for resonance. Certain vibrational frequencies of molecules will produce resonance. That is to say, these molecules will vibrate with large amplitudes in conjunction with special vibration wavelengths. The same segments must fit properly on the extended body of the molecule such that nodes and antinodes exist at positions demanded by the constraints of the molecule. In a very real sense, it may be said that genes, for example, are particles that are

confined to finite regions of space and are bound particles. Other examples of bound particles are gas molecules in a closed container and electrons in atoms. The de Broglie wave that represents a bound particle will undergo resonance within a confinement region when wavelengths fit properly into the region. This represents a stationary state of the system. Indeed, it appears that molecules in cells are not free to do what they want, but are bound by various constraints of the systems which confine them and regulate their activity. It seems possible that photon–phonon transductions may induce resonant vibratory states (microgravitational quantum vibrational interactions) which may amplify to enhance ΔE (available energy for ATP formation) and the diminution of entropic states in cells and in intercellular spaces. Since the total energy of a particle (i.e., its rest mass energy plus its translational kinetic energy intrinsic to the particle) is represented by E a convenient expression for E is

$$E = mc^2, \quad [1]$$

where c is the velocity of light. The induced electromotive force (emf) V in an electrically conducting carrier of length L moving with velocity v through a magnetic field with intensity B is given by Faraday's law,

$$V = BvL. \quad [2]$$

Induced electromotive force (emf) V is energy per unit charge, q, i.e.,

$$V = \frac{E}{q}. \quad [3]$$

The following equation is arrived at by equating the previous two equations:

$$E = BvLq. \quad [4]$$

Jacobson's equation, can be arrived at by equating the first and the fourth equations:

$$mc^2 = BvLq. \quad [5]$$

The above equation applies when B is orthogonal to v and the long axis of L. It is proposed that we may select B (magnitude of B) and apply the magnetic component of the force moving through L whose energy is equal to the specific intrinsic energy mc^2 of any particle. V may be any inertial velocity, e.g., earth's orbital velocity. Since the velocity of the magnetic field is c, the interaction between a magnetic field and a material particle is independent of the inertial frame of the earth. Due to the great velocity of cosmic inertial systems, i.e., 3×10^6 cm/s for earth's orbital velocity, there may be a spontaneous interaction resulting in the promulgation of a photon–phonon transduction or virtual photonic flux in a microgravitational interaction and a consequential quantized vibration of lattice structures with reorientation of magnetic moments and spin angular momenta of fundamental particles, e.g., electrons, nucleons and atoms. The rationale for the unidimensionality of the biological system or 'carrier' is adapted from Einstein, who viewed the largest dimension of all three-dimensional objects as the one most closely associated with its velocity (24–27). The dualism of the wave-particle nature of reality is analogous to the matter waves of de Broglie, represented by

$$\lambda = \frac{h}{p} = \frac{h}{mv}$$

and the fundamental Einstein equation (3–7)

$$W = hf.$$

Adenosinetriphosphate (ATP) is a coenzyme and one of the most important compounds in the metabolism of all organisms, since it serves as a coupling agent between different enzymatic reactions. ATP is a powerful donor of phosphate groups to suitable acceptors because of the pyrophosphate nature of the bonds between its three phosphates. ATP serves as the immediate source of energy for the mechanical work performed by muscle. In its presence, the muscle protein actomysin contracts with the formation of adenosinediphosphate and inorganic phosphate. ATP is also involved with the activation of amino acids, a necessary step in the synthesis of protein. In metabolism, ATP is generated from ADP and inorganic phosphate mainly as a consequence of energy-yielding oxidation–reduction reactions. In respiration, ATP is generated during the transport of electrons from the substrate to oxygen via the cytochrome system. Now, when the electrical potential changes across the faces of a lattice structure such as a protein, a small mechanical deformation occurs. Franco Bistolfi reports that recent studies have proved that proteins containing more than one α-helix have a nearly spherical polyhedron geometry. This structure gives the same proteins quasi-crystalline characteristics and explains the piezoelectric properties now under discussion. This deformation causes reorientation of the molecules and atoms making up the structure. This reorientation, in turn, can make atoms and molecules jump from one point to another. One example may be biophotonic emissions which are extremely weak and range from close UV to lower radio frequency, wherein the unwinding and rewinding of the DNA double helix are accompanied by rupture and recreation of hydrogen bonds (43,51,52).

It has been shown that many human tissues may be piezoelectric. Debate is ongoing about which tissues and structures may be piezoelectric, and indeed whether all are piezoelectric to a greater or lesser extent. Many researchers agree that genes, cytoskeletal structures such as centrioles, α-helices such as those in nails and hair,

collagen and bone are piezoelectric. In other words, electromagnetic oscillations acting on these structures are converted to mechanical vibrations in the structures themselves, and vice versa. Continuing this concept, it could be a possibility that the structures of genes, growth factors, proteins, hormones, RNA and other important molecules are influenced through the macro mechanisms of biochemical activity. Based on the concept of biological piezoelectricity, every biochemical interaction could be associated with concomitant reorientation of electromagnetic fields. Therefore, biomolecular resonances may influence the energetic states of coherent charged particles and transfer energy from the domain of the quantum vacuum through microgravitational processes which increase ΔE or available free energy for ATP production and domination of conformational entropic states which are deleterious to normal electrophysiological states.

HYPOTHETICAL CONSTRUCTS AND COROLLARIES

The mechanism underpinning biological effects demonstrated secondary to impingement of picoTesla magnetic fields upon organisms are hypothesized to be based in the subatomic realm. There is a connection between the particles that comprise atoms (which are themselves permanent spinning magnets) and the cells that comprise us. It seems logical to presuppose that every level of structure and function underlies another and forms part of the basis for perceived function. If an applied field is physiologic, or natural to the system, then there may be reorientation of order and coherence in tissue. Improved cooperativity of systems and coherent charged states may be manifest as ionic channels are influenced, e.g., calcium influx and efflux.

There have been several studies suggesting that there must be several orders of magnitude amplification of initial EM stimuli which are recognized at the cell membrane surface needed to account for observed effects (8,9,19,30–32,38–40,82). These included: EM field far weaker than the EEG that influence circadian rhythms in man and birds reported by Wever (75), and time estimation in monkeys observed by Gavalas-Medici et al. (76) and navigation and predation in sharks and rays studied by Kalmijn (77). Following are some of the studies, observations, and proposed models that may account for these, as well as the studies in which pT ELF magnetic fields demonstrated significant nerve regenerative effects (10). Calcium levels are high in the fluid around cells (2.0 mM), and very low in the cytoplasm (10^{-7} M), while entry of micromolar amounts of calcium into the cell is powerful stimulus to intracellular systems, including activation of major enzyme systems. In order for the interactions to occur at athermal levels (i.e., below kT) in biological substrates and with EM fields at the low frequency, Turing presented biomolecular models exhibiting cooperative patterns of organization (78). Othmer and Scriven extended these cooperative organization models to include cellular networks (79). In biologic systems, these cooperative dynamic patterns are initiated and sustained by continuous inputs of energy. They are termed as 'dissipative' processes and occur at far from equilibrium states with respect at least to one important parameter in the system of Katchalsky and Curran (80). These non-equilibrium processes are characterized by resonant or 'window' phenomena, and are associated with highly cooperative modulation of Ca binding at sites on terminals of stranded glycoproteins. These non linear vibrational states involve solitary waves similar to those proposed by Davydov moving in sequence down the length of glycoprotein and lipoprotein molecules. Solitons may arouse the interaction of phonons and excitons along linear molecules that result in nonlinear molecular vibrations. Adey (8,11,15,36,81), using the solitons and the non-linear models, attempted to explain how ELF fields millions of times weaker than the transmembrane gradient of 10^5 V/cm, can modulate cell response to surface stimuli. However, with the intramembranous proteins (IMPs) crossing the phospholipid bilayer being hydrophobic, and the necessity for photonic recycling of cell surface interaction after dissipation of energetic states, their model appears to further require structural and thermodynamic properties to maintain the necessary and sufficient energy (ΔE) sources for such an amplification (15). ELF fields apparently modulate surface electrochemical events, amplifying the trigger action of the ligand–receptor bond. Even though one accepts that the ligand–receptor association alters the conformation of the extruding portion of the IMPs at cellular surfaces, and that this change is communicated to the cytoplasm by transmembranous helical segments, by receptor aggregation, or by nonlinear vibration of helical proteins with soliton generation, one still must account for the (10^{12}) differential between the photonic energy of a ELF wave and the Boltzman energy kT. When an extremely weak electromagnetic field (the magnetic component of which is in pT range) is impinging upon a biological system, the magnetic component will pass through the membrane while the electric component is sharply attenuated due to the high impedance. According to Clegg, the ligand–receptor association is followed by cytoskeletal-mediated events and by the production of a 2nd messenger (cAMP or cGMP) by activation of the cyclase enzyme in the membrane itself or in its proximity (16). The microtrabecular reticulum establishes connections with membrane receptors and other structures in the cytoplasm (13,14). These reticulum-receptor

connections result in an excellent means of intracellular communication. The microtrabecular reticulum consists of actin filaments and ATP molecules. It has been suggested that this may supply the necessary energy (ΔE) to activate the cyclase enzyme which requires a large input to produce the cyclic nucleotides (2nd messengers). Clegg stated that the growth sites of actin filaments are very close or directly connected to specific plasma receptors. The effect is the facilitation of the synthesis of a 2nd messenger and the transmission of external stimuli which reach the surfaces of cells directly, and rapidly communicate with the entire cell. Consequently extremely weak stimuli may be amplified and athermal effects by non-ionizing radiation may be produced (17). One may rationalize that magnetic fields produce piezoelectricity through the intracellular matrix, converting electromagnetic oscillations to mechanical vibrations (i.e., photon–phonon transductions), to induce molecular vibrations of frequencies specifically responsible for biological amplifications of extremely weak triggers at the membrane surface, as well as junctions. The frequency of the oscillating phenomenon related to hydrogen bonds is described by Bistolfi. The frequencies appear to be limited in the vast infrared (IR) frequency band, from near IR (10^{14} Hz) to far IR neighboring mm MW (10^{12}–10^{11} Hz). The hydrogen bonds of considerable importance are those in proteins and DNA. They have oscillation frequencies in the lower range at about 10^{11} Hz for DNA hydrogen bonds and around 10^{12} Hz for some proteins such as hemoglobin, lysozyme, keratin, poly-L-alanine and several poly crystalline aminoacids (15). DNA and protein hydrogen bonds, therefore, may be considered as centers of EM radiation emission in the range from the mm microwaves to the far IR. Piezoelectricity may be the common denominator for the aspecific actions of the various non-ionizing, order-inducing biological physical effects. Piezoelectric mechanisms may be present in all physiological processes. Examples are cells specialized in reception of external stimuli (heat, pressure and sound). These cells may convert the special types of energy and are sensitive to the energy (ΔE) which is order inducing and regulates the ATP metabolic engine. Various structures are thought to be piezoelectric, such as bone tissue, blood vessel walls, collagen fibers, keratin, albumin, and globulin, lipo- and glycoproteins, nucleoproteins, histones, DNA and microtubules. Recent studies by Murzin and Finkelstein (18) have reported that proteins containing more than one α-helix have a nearly spherical polyhedron geometry. This structure renders the proteins quasi-crystalline, one of the characteristics that is associated with their being piezoelectric. Many of the molecules which are recognized as piezoelectric have α-helices present, and have an ordered polypeptide structure and a set of ordered dipoles which correspond to the definition of electret. Electrets are parallel molecular assemblies where the microscopic subunits and the whole unit have stable and permanently oriented dipoles. Electrets fulfill the requirement for an ideal cooperative system described by Adey, in which the system's microcomponents are: coherent, with congruent oscillatory trajectories, and ordered. In a near ideal cooperative system, due to the ordered structure, the entropy is retained at a minimum and biologically ordered free energy (ΔE) is maximized and made available by the interaction with the external stimuli and its components for required amplification and driving the metabolic ATP engine. α-helices seem designed for vectorialized conduction of phonon like energy pulses from the centers of energy release (redox reactions, ATP hydrolysis) to the site where it is used. α-helices can therefore be compared to piezoelectric polypeptide springs able to transform chemical and electromagnetic energy into mechanical energy, and mechanical energy into electromagnetic energy. Thus the amplification of weak triggers by a factor of about 10^{12} is thought to occur through mediation of the magnetic component (of EM field) by piezoelectric structures both extra cellularly and intracellularly. Since the magnetic component may pass freely through the extremely high impedance (for electric component of EM field) of the lipo-protein domain of the cell membrane, the amplifications secondary to photon–phonon transductions are made possible, and provide reduction of configurational entropy with available free energy (ΔE) to enable the utilization of the ATP-driven metabolic engine in promotion of growth, repair, and balanced function.

Responses of critical molecules to certain magnetic field signals may include enhanced vibrational amplitudes, increased quanta of thermal energies, and order producing interactions. For example, NGF may be considered as an 'electret-like', i.e., piezoelectric, semicrystalline structure, and can be defined physically as an aggregation of charged particles whose integrated vectors have a quantum magnetic moments, and can be influenced with an extreme sensitivity by external magnetic fields. In general these interactions possibly reorient submolecular magnetic domains and improve communications between and among critical molecules that comprise and engender the dance of life.

CORRELATIONS TO OTHER RESONANCE PHENOMENA

The mechanism underpinning reported biological effects secondary to exposure with ELF (extremely low frequency), non-ionizing radiation (NIRs) of such low photonic energies (10^{12} below kT) to be incapable of

heating tissue is proposed. Heating has long been thought to be the basic mechanism by which radiant energy may produce biological effects. Perhaps beneath the cloak of biochemical events there are concomitant electromagnetic interactions, especially because all atoms are themselves permanent spinning magnets; and as Einstein said, all matter is ultimately composed of elementary electric charges (28,44).

Additionally, Einstein stated in his 1920 University of Leyden Address, 'Since according to our present conceptions the elementary particles of matter are also, in their essence nothing else than condensations of the electromagnetic field, our present view of the universe presents two realities which are completely separated from each other conceptually, although connected causally, namely, gravitational ether and electromagnetic field, or as they might also be called—space and matter' (3,22,28,29,44).

It is hypothesized that the descriptor undercurrent in NIR bioeffects may be piezoelectricity via structures within the cell as well as extracellular matrix. The fundamental interaction postulated relates to mechanical electromagnetic photon–phonon transduction or conversion; that is, the conversion of electromagnetic oscillations into mechanical vibration and vice versa. In order to make educated speculations about the amplitudes and frequencies to use in experiment, it is necessary to create a mathematical structure to account for physical events (45,46). Recent data, linking very weak electrical currents of about a microampere to possible nerve regeneration (41,42) and reports of picoTesla range magnetic fields utilized to treat neurological patients (4,6,7,10,2,21,49) along with classical work by D. Cohen at MIT which measured the picoTesla (pT) magnetic fields associated with the human brain and heart are considered supportive (47).

The objective is to produce mechanical vibrations in selected critical molecules through externally, applied electromagnetic oscillations, or waves. Therefore, it is necessary to mathematically associate waves and particles. The next logical step is to revisit Einstein, Planck and De Broglie, thus recapitulating:

$$E = mc^2, \quad [1]$$

where E is energy, m is mass and c is the velocity of light. Also,

$$E = hf, \quad [6]$$

where E is energy, h is Planck's constant and f is frequency. Now,

$$c = f\lambda, \quad [7]$$

where c is the velocity of light, f is the frequency and λ is the wavelength of electromagnetic waves. Combining Eqs. [6] and [7],

$$E = \frac{hc}{\lambda}. \quad [8]$$

Now, combining Eqs. [1] and [8] we derive,

$$mc^2 = \frac{hc}{\lambda}. \quad [9]$$

Dividing by c, the velocity of light, we then see De Broglie's equation,

$$mc = \frac{h}{\lambda}. \quad [10]$$

The left side of Eq. [10] represents the momentum of a particle, whereas the right side of Eq. [10] represents that particle as a wave – with wavelength λ. The foregoing appears interesting because we have a single equation describing on the one hand a particle and on the other hand a wave. We may consider that perhaps there is a way to mathematically relate the quantitative parameters of an electromagnetic signal to specific target masses of critical molecules to increase their amplitudes of vibration, coherently, improve homeostasis, and decrease configurational entropy thus increasing available energy (ΔE) for renormalization of structure and function.

Generalizing Eq. [10] by letting $c = v$ (any velocity) we write,

$$mv = \frac{h}{\lambda}. \quad [11]$$

String theory has won some favor within the physical community and has been discussed by Waldrop (23).

Hence, we may allow λ to be the circumference of a single loop of string with radius L, as in string theory.

$$\lambda = 2\pi L. \quad [12]$$

Combining Eqs. [11] and [12],

$$mv = \frac{h}{2\pi L}. \quad [13]$$

Rearranging Eq. [13],

$$vL = \frac{h}{2\pi m}. \quad [14]$$

Now, adding a charge q either separate or representational of m and a magnetic flux density B to the system we derive,

$$BvLq = \frac{qhB}{2\pi m}. \quad [15]$$

Since the electronic g factor is equal to 2.002322 we may write,

$$E = BvLq = \frac{g_e qhB}{4\pi m}, \quad [16]$$

where g_e is the electronic g factor.

The Zeeman energy (magnetic resonance) term

$$\frac{g_e qhB}{4\pi m} = BvLq$$

an expression derived from De Broglie's particle-wave equation. It seems possible then to write a different particle-wave equation, directly derived from fundamental physical laws. Combining Eqs. [1] and [16] we get

$$mc^2 = BvLq. \quad [17]$$

This equation appears unusual, especially because the presence of v and q provoke questions, even if one were to allow L to be equal to the length of the biological system. However Faraday's law of a straight conductor of length L moving through a flux density B with velocity v to produce an electromotive force V within the conductor, previously stated in Eq. [2] demonstrates that a Lorentz Force is propitiated within L.

V is expressed in volts (MKS) or ab-volts (CGS), and is defined as *energy per unit charge*, stated in Eq. [3]. When combining Eqs. [2] and [3] we derived,

$$E = BvLq$$

as in Eq. [16], which demonstrates precisely the equivalency of Zeeman energy to $BvLq$ on a generic basis.

Now the dilemma is this: Is the wave energy produced by an electromagnetic interaction with a biosystem equal to the intrinsic energy (mc^2) of a critical molecule? If so, one could wonder whether m might be the mass of a molecule, but how then could we account for v and q? What quantitative values might they have?

Referring to Eq. [3], *electromotive force is defined as energy per unit charge*. The thought strikes, 'What would happen if we normalize charge $q = 1$?' Then, we would not need to identify charge q in any quantitative manner within the biological system. We are faced with the possibility then that in the CGS unitary system of gravitation:

$$mc^2 = BvLq, \quad [18]$$

when $q = 1$.

If so, what value could v have that would represent reality? Is it not true that we travel with the earth as it follows a regular orbital path about our Sun? Are we not traveling at the same velocity as the earth, given a non-terrestrial co-ordinate system of reference? Supposing that the answer to the foregoing is yes, the question remains, 'As a primary example, does the geomagnetic field, the steady magnetic field of the earth, also travel with the earth? If it does, how then could the earth otherwise affect biological systems but to induce weak electric currents in moving tissue such as red blood cells which contain ferromagnetic material'. However, if we accept Faraday's notion that any conductor moving through a magnetic field will induce a force within the conductor, then, according to the theory of special relativity, the geomagnetic field is not moving with the earth, and forces must be generated within biological systems. Perhaps v could equal the orbital velocity of the earth? The key seems to be the fact that electromagnetic waves always travel at the velocity of light – *independent of their inertial frame of reference.* And if that is true, i.e., the geomagnetic field does not travel with the earth but is incessantly re-created by the earth, then any conductor just sitting on the earth in the geomagnetic field must have a force induced therein. Yet we cannot measure any electromotive force or see any ostensible effect of such a supposed force? If such a force exists, where is it and how could it produce bioeffects, especially secondary to a picoTesla range magnetic field?

We have these ideas about space and matter, about mechanical electromagnetic photon–phonon transductions and about piezoelectricity. These considerations point to a gravity wave, something very difficult to detect indeed. We cannot look for a gravity wave but we may look for its effects from a theoretical standpoint. We are ready to make our calculations, but first comes the decision about which unitary system ought to be tested first. An analogy between Maxwell's electromagnetism theory and Einstein's theory of gravity is that just as electromagnetic (EM) waves are created by the vibration of electric charges, a gravity wave might travel through space to shake other masses. The notion that the gravity wave is the basis of photon–phonon transductions in biological piezoelectricity involving extremely weak signals represents a possibility explicating the nexus in the multi-magnitude and multi-faceted biological amplification process.

It then appears that if we are to shake the metric of space–time itself, the forces we should deal with most directly are electrostatic in nature, most especially since our hypothesis depends upon a force that cannot be measured directly or even detected.

The decision is made to employ the centimeter gram second (CGS) unitary system because the unit of charge in the meter kilogram second (MKS) system of units is defined in terms of force between moving charges rather than the electrostatic force between charges as in the CGS system of units. We proceed to calculate, according to Eq. [18], the B field associated with the length of a mouse L, the orbital velocity of the earth v and target mass m – nerve growth factor, (NGF), a molecule important in nerve regeneration. Nerve growth factor has a molecular weight of 26.5 kDa, the mean orbital velocity of the earth is about 18.5 miles per second (3×10^6 cm s^{-1}), and the average length of a small mouse is 10 cm. The velocity of electromagnetic waves c in CGS is 3×10^{10} cm s^{-1}. The normalized unit of charge, $q = 1$, represents 1 ab-C in the CGS system of units. 26.5 kDa is equal to 4.4255×10^{-20} g as 1 Da is equal to 1.67262×10^{-24} g (mass of a proton). Now we can test our hypothesis:

$$4.4255 \times 10^{-20}\,\mathrm{g} \cdot 9 \times 10^{20}\,\mathrm{cm^2\,s^{-2}} = 1.32765 \times 10^{-6}\,\mathrm{G} \cdot 3 \times 10^{6}\,\mathrm{cm\,s^{-1}} \cdot 10\,\mathrm{cm} \cdot 1\,\text{ab-C}, \quad [19a]$$

$$\text{NGF molecular weight} \cdot c^2 = B \cdot v(\text{ earth orbital velocity }) \cdot L(\text{mouse}) \cdot q \times (\text{unit electric charge}) \ldots \quad [19b]$$

(This calculation was made for the mice motor meuropathy study the data from which is presented herein.)

This is an interesting calculation because when we substitute the height of an average human, about 5 feet 8 in. or 1.7×10^2 cm, for L we see:

$$4.4255 \times 10^{-20}\,\mathrm{g} \cdot 9 \times 10^{20}\,\mathrm{cm^2\,s^{-2}} = 7.8097 \times 10^{-8}\,\mathrm{G} \cdot 3 \times 10^{6}\,\mathrm{cm\,s^{-1}} \cdot 1.7 \times 10^{2}\,\mathrm{cm} \cdot 1\,\text{ab-C} \quad [20a]$$

$$m \cdot c^2 = B \cdot v \cdot L \cdot q. \quad [20b]$$

Perhaps fortuitous, but the calculated B field for the human is precisely the amplitude of the magnetic field used to treat neurological disorders (20,21,48).

Combining Eqs. [15] and [17] we then desired,

$$mc^2 = \frac{qmc^2 tB}{2\pi m}. \quad [21]$$

Dividing both sides of Eq. [21] by mc^2 and by t we get

$$\text{Frequency}(f) = \frac{qB}{2\pi m}. \quad [22]$$

Eq. [22] is the equation for cyclotron resonance. Since Eq. [22] is an MKS expression, we converted 1.32765×10^{-6} G in CGS to the MKS equivalent 1.32765×10^{-10} T, as 10^4 G = 1 T unit of magnetic flux density. Now, q was normalized in the CGS system of units, $q = 1$ ab-C, whereas 1 ab-C is equal to 10 C in MKS; we discern that q in Eq. [22] has also to be normalized according to the same standard set by Eq. [18], that is, the charge of the electron has to be multiplied by a factor of 10. Thus, e is the electronic charge, $e = 1.6 \times 10^{-19}$ C. Therefore,

$$1.6 \times 10^{-18}\,\mathrm{C} = 1.6 \times 10^{-19}\,\mathrm{C} \cdot 10 = q. \quad [23]$$

Holding the standard for normalization of charge in CGS.

Then, we proceed to do the calculation:

$$f = \frac{1.6 \times 10^{-18}\,\mathrm{C} \cdot 1.32765 \times 10^{-10}\,\mathrm{T}}{2\pi(6.2832) \cdot 9.11 \times 10^{-31}\,\mathrm{kg}} = 37.111\,\mathrm{Hz}, \quad [24]$$

where q is adjusted for normalization from the charge of an electron in C (MKS) and the rest mass of the electron is 9.11×10^{-31} kg. Utilizing target mass (NGF), we note that 1.28×10^{-6} G with frequency 35.7 Hz was utilized in the in vivo motor-neuropathy study herein presented in Table 1. Small variations in signal represents an attempt to account for other neighboring target masses like interferon and growth associated protein (GAP). We proceeded as such in our tabulation of target masses' amplitudes and associated frequencies of EM signaling hoping for a positive outcome. And, these data suggest that further research is indicated concerning the exploration of possible physical mechanisms which might prove to be the underpinning of bioeffects from non-ionizing, radiation and biological piezoelectricity.

Finally, if the electronic charge were to be used as a unit charge,

$$1.6 \times 10^{-19}\,\mathrm{C} \cdot 0.1 = 1.6 \times 10^{-20}\,\text{ab-C},$$

we must normalize q to convert from CGS to MKS (for $f = 8B/2\pi m$) by multiplying 1.6×10^{-20} ab-C e by a factor of 10, as 1 ab-C = 10 C.

Therefore, we are at liberty to utilize $f = qB/2\pi m$ as a CGS expression, and we note:

Table 1 The electromagnetic fields microgauss and milligauss settings as applied to Group 2 IDPN treated mice and mass (kilo Dalton, kDa) of molecules

Microgauss		Milligauss	
Intensity (G)	Frequency (Hz)	Intensity (G)	Frequency (Hz)
9.69×10^{-6}	271.1	0.17×10^{-3}	2.55
8.77×10^{-6}	244.7	0.0875×10^{-3}	1.31
7.7×10^{-6}	214.8	0.0774×10^{-3}	1.15
5.8×10^{-6}	161.8	0.055×10^{-3}	0.82
4.7×10^{-6}	131.1	0.043×10^{-3}	0.64
3.6×10^{-6}	100.4	0.034×10^{-3}	0.5
2.98×10^{-6}	83.1	0.0272×10^{-3}	0.41
2.55×10^{-6}	71.1	0.0221×10^{-3}	0.33
2.14×10^{-6}	59.37	0.017×10^{-3}	0.254
1.28×10^{-6}	35.7	0.014×10^{-3}	0.21
1.14×10^{-6}	31.8	0.0122×10^{-3}	0.183
1×10^{-6}	27.9	0.011×10^{-3}	0.158

Mass of molecules (kDa): Dynein-1200, Kinesin-350, Microtubule Associated Protein (MAP)-280, Neurofilament-200, Tubulin-110, Chloinesterase-75, Growth Associated Protein (GAP)-43, Platelet Derived Growth Factor (PDGF)-30, Nerve Growth Factor (NGF)-26.5, Calmodulin-16.5, ATP-0.503, Acetylcholine-0.146.

$$f = \frac{1.6 \times 10^{-19}\,\text{ab-C} \cdot 1.32765 \times 10^{-6}\,\text{G}}{2\pi(6.2832) \cdot 9.11 \times 10^{-28}\,\text{g}} = 37.111\,\text{Hz}. \quad [25]$$

Thus, in CGS, 1.6×10^{-20} ab-C $\times 10 = 1.6 \times 10^{-19}$ ab-C normalizes q for $f = qB/2\pi m$, an MKS expression describing the force between moving charges as discussed before.

Now, in the equation:

$$f = \frac{BvLq}{h}, \quad [26]$$

where h is defined by $mc^2 \cdot t$, mc^2 represents the *wave energy of the target mass* when m is, for example, nerve growth factor. Furthermore, when q is normalized in $f = qB/2\pi m$ and m is the target mass, while B is the deserved physiologic flux density from $mc^2 = BvLq$, then f represents the induced molecular vibrational frequency of the target molecule when resonance is achevied and the oscilatory vibrations of m increases in amplitude, thus

$$f = \frac{(1\,\text{ab-C})(7.8 \times 10^{-8}\,\text{G})}{(2\pi)4.4 \times 10^{-20}\text{g(NGF)}} = 2.8 \times 10^{11}\,\text{Hz} \sim m.v.f\,(\text{DNA}). \quad [27]$$

Now to explicate the relation of the two approaches with $mc^2 = BvLq$, when q is normalized as e the charge of an electron, then 1.6×10^{-19} C $= 1.6 \times 10^{-20}$ ab-C, m is the rest mass of the electron at 9.11×10^{-28} g, v is earth orbital velocity, L is the height of a human and c is $3 \times 10^{10}\,\text{cm s}^{-1}$. Since cyclotron resonance takes into account forces between moving charges and is an MKS expression,

$$1.6 \times 10^{-20}\,\text{ab-C} \times 10 = 1.6 \times 10^{-19}\,\text{ab-C} = q,$$

$$9.11 \times 10^{-28}\,\text{g} \cdot 9 \times 10^{20}\,\text{cm}^2\,\text{s}^{-2} = B \cdot 3 \times 10^{6}\,\text{cm s}^{-1} \cdot 1.7 \times 10^{2}\,\text{cm} \cdot 1.6 \times 10^{-19}\,\text{ab-C},$$

$$\text{e mass} \cdot \text{c}^2 = \text{EO} \cdot \text{HL} \cdot \text{unit charge}$$

Calculating:

$$B = \frac{82 \times 10^{-8}\,\text{cm}^2\,\text{s}^{-2}\,\text{g}}{8.16 \times 10^{-11}\,\text{cm}^2\,\text{s}^{-1}\,\text{ab-C}} \cong 10^4\,\text{G}, \quad [28]$$

which represents a typical MRI signal. Finally, when we normalize charge e heretofore delineated,

$$f = \frac{1.6 \times 10^{-19}\text{ab-C} \cdot 10^4\,\text{G}}{(2\pi)9.11 \times 10^{-28}\,\text{g}} = 2.8 \times 10^{11}\,\text{Hz} \quad [29]$$

approximately the same frequency as Eq. [27], indeed a molecular vibrational frequency of critical molecules in the human genome as well as associated particles.

$$10^5\ \text{G gives us}\ \approx 10^{12}\,\text{Hz (protein)}.$$

The biological-electromagnetic affectation generally involves an integration of factors over time to produce manifestation of amplification of weak signal transductions (33,35,37,50,53–55). The portion of receptor proteins which lie in plasma membranes are comprised of a helix of about six turns, and are composed entirely of hydrophobic amino acids, incapable of hydrogen bonding or ionic conduction, yet mediate the rapid transfer of ions. Conversion of electromagnetic oscillations to mechanical vibrations and vice versa; i.e., piezoelectricity, in this regard, is critically important. Landau levels reorient and Fermi energies rise to account for the subtle pressure of weak, low intensity fields on the external manifold. When E is the photon energy, h is Planck's constant and f is the frequency of the radiation:

$$E = hf \quad [6]$$

When $f = 16$ Hz, an important Ca^{2+} window, then

$$E = 6.626 \times 10^{-34}\,\text{Js} \cdot 16\,\text{Hz} = 1.06 \times 10^{-32}\,\text{J} \quad [30]$$

Now, k is a constant equal to R/N, where R is the universal gas constant and N is the Avogadro constant. It has the value 1.380622×10^{-23} JK^{-1}. When K is body temperature, 37 °C or 310 K, then

$$kT = 1.382622 \times 10^{-23}\,\text{JK}^{-1} \cdot 310\,\text{K} = 4.28 \times 10^{-21}\,\text{J}. \quad [31]$$

Therefore, dividing Eq. [31] by Eq. [30] we get

$$\frac{4.28 \times 10^{-21}\,\text{J}}{1.06 \times 10^{-32}\,\text{J}} = 4.04 \times 10^{11} \quad [32]$$

4.04×10^{11} Hz is about the molecular vibrational frequency of the DNA hydrogen bonds which connect the nucleotides, and represents a necessary quantitative amplification of a weak trigger.

RATIONALE FOR CYCLOTRON RESONANCE

Finally, the rationale for utilizing the ion cyclotron resonance equation,

$$f = \frac{qB}{2\pi m}$$

to determine frequencies associated with steady magnetic field B as derived from Jacobson Resonance is as follows:

While amplitude resonance is the basis for

$$mc^2 = BvLq$$

it is often necessary in clinical situations to impose a changing field B to re-adjust circadian rythmicity concomitant and directly associated with (d.c.) physiologic magnetic profile B. Thus, when changing physiologic magnetic fields such as 5×10^{-8} G are maintained externally about current carrying semi-conductive organismic body parts (or whole organism) through placement in solenoidal or Helmholtz configurational environments,

there is a resultant emf generated based upon the piezoelectric and Hall effects, across said conductive bodies; until the transverse electrostatic field E_e within the conductive biosystem is equal and opposite to the non-electrostatic field E_n. This makes the final transverse current equal to zero (the conductive body being on 'open-circuit' in the transverse direction). Therefore, the induction of equilibrium of charge is accomplished congruent to certain rythmicity, which therein rearranges sub-molecular magnetic domains. This brings about bio-intrinsic production of the *B* field to d.c. status within the organism to then correspond in amplitude to the frequency of polarity change extrinsically impinged with a.c. *B* field. This may cause 'gene jumping' as electron and proton magnetic moments reorient the atomic semi-crystalline lattice structures of malaligned genes and associated structures, e.g., oncogenes, as well as other quantum semi-conductive masses such as viral nucleic acids (free strands); which regulate therein metabolic processes responsible for maintaining physiologic homeostasis, normal energy transport systems, reflected by hormonal and enzymatic normalcy, and health of the organism.

Recapitulating,

$$mc^2 = BvLq$$

is an expression fundamentally concerned with the d.c. field *B* that is intrinsically produced by the biological system and is associated with the cyclotron resonance frequencies generally ranging from extreme elf to 100 Hz in bio-systems supporting physiologic circadian rhythms. When a changing *B* field is impinged upon a bio-system or part thereof with appropriate rythmicity the response of the organism is to intrinsically renormalize the (d.c.) magnetic profile, which in conjunction with changing, intrinsic electric fields produce normalcy in fluctuating physiologic fields corresponding in amplitude to the externally sourced field (12,22,23). In this manner the cyclotron resonance is utilized to renormalize magnetic profiles and their (d.c.) and (a.c.) status. Finally, the center of the fixed co-ordinate system of reference for such inertial velocities as earth orbital is necessarily our sun; while other co-ordinate systems of reference may also be used, e.g., star cluster velocity with the Milky Way Galaxy used as the referential frame. The rationale includes Einstein's view that while there is no absolute reference system all systems that share translational motion may be related in actuality.

RECOVERY OF MOTORNEUROPATHY IN MICE BY APPLIED ELECTROMAGNETIC FIELD

Introduction

The energy state and bioelectric potential of nerves may be modulated by electromagnetic fields. The field intensity and gradients were calculated considering subcellular components vital for nerve function.

The effect of uniform electromagnetic fields (EMF) on the restoration of forelimb grip strength and radial nerve ultrastructure was studied in mice with motorneuropathy. The motorneuropathy was induced by the administration of a neurotoxin, 0.62% 3,3′-iminodipropionitrile (IDPN), in drinking water for 9 1/2 weeks. Forelimb grip strength (lb) of mice as measured by a force gauge meter declined to 47% compared to the control group ($p < 0.004$). The IDPN treated group without any magnetic field exposure persisted to have a 56% decrease in grip strength and radial nerve electronmicrographs showed axonal demyelination, mitochondria in an orthodox state of conformation, and uneven dispersion of neurofilaments and microtubules. In contrast, one IDPN treated group was treated with applied magnetic flux densities and frequencies that were calculated on the basis of the mass of molecules vital to nerve function. During field exposure mice were held in a perforated Lucite box placed in a Resonator that generated the EMF between the centers of two 18 in. discs, 9 in. apart containing copper coils in Helmholtz configuration. EMF was applied twice weekly for 8 1/2 weeks that resulted in as much as 87% recovery ($p < 0.05$) of grip strength that was sustained after the termination of exposure at an 82% level until the 27th week of observation. The EMF exposed group also exhibited axonal remyelination, condensed state of mitochondria, and evenly dispersed neurofilaments and microtubules consistent with grip strength recovery. These results are the first to demonstrate a biological effect of EMF in vivo on the restoration of subcellular structures required for nerve impulse conduction and metabolism in nerves and consequently a grip strength recovery from motorneuropathy, under controlled experimental conditions.

Current experimental and clinical findings have shown a measurable effect of electromagnetic fields (EMF) on nerve repair, regeneration, growth and pain alleviation. The weak pulsed magnetic fields (PMF) as well as the direct current (d.c.) field have distinct regenerative effects on nerves and also wound healing actions (33,34,41,42).

The EMF in very low ranges of picoTesla (pT) amplitude have been used in the amelioration of neurological disorders (7,12,48,49,83,84) and chronic osteoarthritic pain conditions (21,56). Recently, narrow spectrum infrared wavelengths that are within the frequency range of the radiation emitted by the human body have shown to normalize diabetic metabolism by restoring the control mechanisms of the hypothalamus for the sympathetic and parasympathetic nervous system (57). These studies suggest certain biological responses were elicited

by EMF exposure. An interaction of extremely low frequency EMF in-vitro at a cellular level has also been shown in the alteration of polypeptide synthesis in salivary gland cells (58), glycolytic activity in fibroblasts (59) and in sodium-potassium ATPase enzyme systems in cells (60). It was suggested by Adey (61,62) that the interaction between the endogenous electromagnetic fields with the externally applied EMF of low frequency and amplitude produce biological responses. Secondary to cellular activity each tissue generates a low intensity endogenous electromagnetic field. For example, weak magnetic fields in picoTesla ranges has been measured during alpha rhythm of a normal brain (47).

The rationale of this study is based on the premise that extremely low frequency and weak intensity EMF may supplement the endogenous electromagnetic field and cellular function may be restored from a state of motorneuropathy. A precise correlation between the nature of the nerve dysfunction and its recovery by EMF exposure under controlled experimental conditions remained to be established. Therefore, a study in vivo was conducted on age-matched mice with motorneuropathy induced by the administration of a neurotoxin (3,3′-Iminodipropionitrile (IDPN)) in order to determine the effect of EMF on forelimb grip strength, indicative of nerve functionality.

Methods and materials

Animal study

Thirty, 4 weeks old Sprague–Dawley female mice (Harlan Sprague Dawley, Madison, Wisconsin) were housed, two animals per cage, in an Institutional Animal Care and Use Committee (IACUC) approved Animal Facility under 10 h light and 14 h dark periods with rodent pellet and water provided ad lib. Three groups of 10 mice each, were designated as untreated control Group 1 and experimental Groups 2 and 3. To induce motorneuropathy (63), the experimental groups received a neurotoxin; 0.62% 3,3′Iminodipropionitrile (IDPN) (Cat. No. 31, 730-6. Aldrich Chemical Company, Milwaukee, Wisconsin) in drinking water ad lib for 9 1/2 weeks.

Measurement of forelimb grip strength

A Digital Grip Strength Meter (Model 0167-004L, Columbus Instruments International, Columbus, Ohio) was used to measure forelimb grip strength in mice. The meter displayed current force, peak tension, or peak compression. The meter was adjusted in the tension peak mode to freeze the reading at each trial. The force unit of the meter was selected to measure the grip strength as pounds (lb). The forelimbs of each mouse were placed on the bar and pulled away by the tail until the mouse clung to the bar. The peak force reading was recorded as displayed. The meter was zeroed before each measurement. Three measurements were taken for each mouse on each trial day.

Electromagnetic field exposure

The apparatus used for the generation of EMF consisted of three units, a Resonator, a Function Generator and an Attenuator. The Resonator (Prototype Development Laboratory, Stennis Space Center, Mississippi) consisted of two 18 in. diameter discs separated 9 in. apart made up of laminated foam containing five turns of # 37 gauge copper coils around the disc that produce magnetic fields. The magnetic field was characterized for each set of coils fabricated in the Helmholtz configuration. The field correlation to the Generator was such that one volt signal was equal to 1 mG. The electronic system used the Stanford Ultra Low Distortion Function Generator (Model DS360) that was capable of producing pure sine waves of high frequency and resolution. The Attenuator unit connected in series with the Resonator used the signal produced by the generator to drive the Helmholtz coils. The attenuation range was selected from milligauss (10^{-3}) range to microgauss (10^{-6}). The EMF intensity produced was uniform between the centers of the coils.

The externally applied EMF fields were calculated by using Jacobson's equation (64) and the frequencies by the Cyclotron Resonance equation (9).

The protocols designated for EMF intensities (Gauss) and frequencies (Hertz) were calculated on the basis of the mass in kilo Dalton (kDa) of metabolically vital molecules involved in nerve function (Table 1) using microgauss and milligauss intensity settings that targeted electrons and protons of the cell respectively. The duration of each intensity was 2 min with an interval of 20 seconds between each intensity setting. The total exposure time using microgauss settings was 24 min followed by 24 min with milligauss settings. The control Group 1 was neither given IDPN nor exposed to EMF. Groups 2 and 3 both received IDPN treatment. However, after IDPN treatment only experimental Group 2 received exposure to EMF protocols twice a week for 8 1/2 weeks whereas the mice in IDPN treated Group 3 were kept in the Resonator without any EMF exposure as the placebo. Two experimental mice were placed within a two-chambered perforated 8 in. × 6 in. Lucite box during each EMF exposure period. Forelimb grip strength for all of the groups was monitored during experimental periods ending with the 27th week of observation.

Electron microscopic studies

The radial nerves from forelimb of mice in control Group1 as well as experimental Groups 2 and 3 were

surgically excised after carbon dioxide euthanasia. The nerve samples were processed for electron microscopy. The nerves were fixed in a solution containing 2% glutaraldehyde, 4% paraformaldehyde and 0.02% picric acid in 0.1 M sodium cacodylate overnight at 4 °C. The nerves were then washed thrice with 0.1 M sodium cacodylate followed with a solution of 1% osmium tetroxide–1.5% potassium ferricyanide in water for 60 min at room temperature. The nerves were then treated with 50% ethanol–3% uranyl acetate in solution for 90 min followed by immersion in a gradient of 70–100% ethanol. Nerve samples were kept overnight in 1:1 ratio of absolute ethanol to Spurr's resin solution then in Spurr's resin alone for 4–8 h at room temperature and then overnight in an oven at 60–70 °C. Cross sections of the nerves of 70 nanometer (nm) in thickness were cut by the aid of an ultramicrotome (85).

Statistical analysis of the data

Statistical analysis of grip strength values was performed by a *t* test considering two tailed, unequal variances for calculating the significance between group means (SPSS, Chicago, IL). Statistical significance was assigned at p values of $\leqslant 0.05$. When a significant p value was obtained the ANOVA test was used to ascertain the significant difference between group means. The p value was then accepted at $p \leqslant 0.01$. Data was analyzed on the forelimb grip strength from the start to the end points of the experiments on IDPN treatment and EMF exposure periods. In addition, percent difference in grip strength of each group between the start and end point of each experiment and percent difference between experimental groups and control group were analyzed.

Results

Effect of IDPN on forelimb grip strength of experimental Groups 2 and 3

Prior to IDPN administration, mice showed grip strength values (Group 1-0.1278 ± 0.033, Group 2-0.1333 lb ± 0.026, Group 3-0.1372 ± 0.044) with no significant difference ($p > 0.8$) between the groups (Fig. 1A and B). At the onset of the third week of IDPN treatment, the mice exhibited hyperkinesis followed by a gradual weakening of grip strength as previously observed in an experimental motorneuropathy model in rats (63). Initial fluctuations in grip test values became relatively steady after the third week of IDPN treatment. At the end of 9 1/2 weeks of IDPN treatment, a significant decline in grip strength (Group 2-0.1147 lb ± 0.08, $p < 0.004$, Group 3-

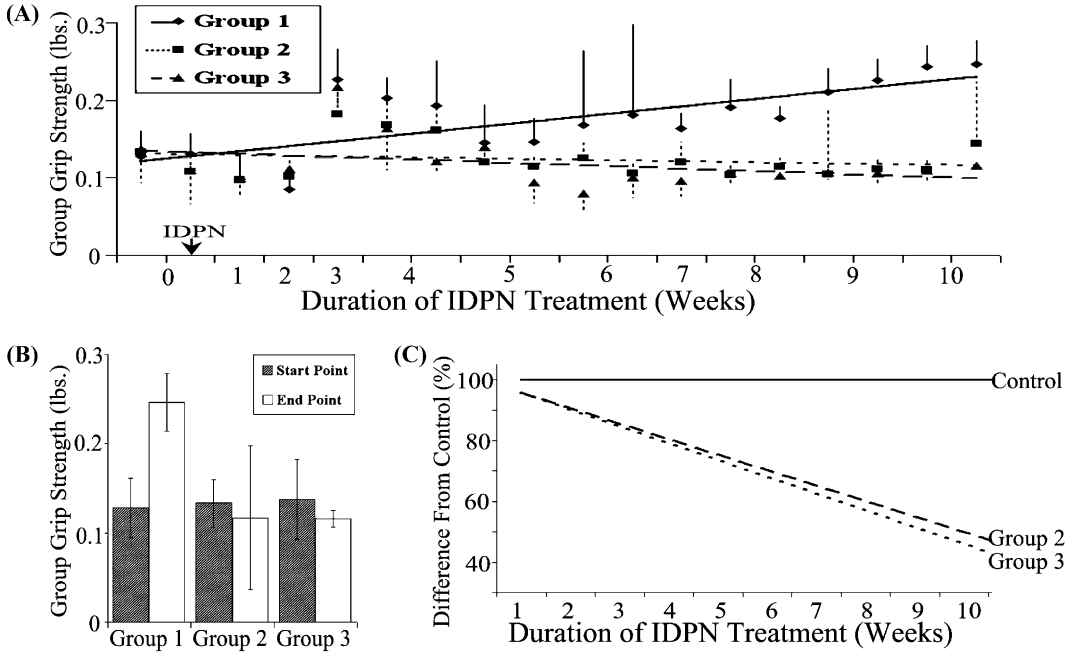

Fig. 1 (A) (Top) Grip strength (lb) of mice ($n = 10$) in experimental Groups 2 and 3 during IDPN treatment for 9 1/2 weeks as compared to control Group 1 (mean ± SD). (B) (bottom left) Grip strength (lb) of mice ($n = 10$) at the start and end points of 9 1/2 weeks of IDPN treatment in Group 2 and 3 as compared to control Group 1 (mean ± SD). Percent change between the start and end points of treatment with statistical comparison of the groups. Change of grip strength between start and end of IDPN treatment period: Group 1: 92.5% increase, Group 2: 13.9% decrease, Group 3: 15.5% decrease. Pre-IDPN group difference: $p > 0.8$. Post-IDPN group difference: Groups 1 and 2, $p < 0.004$, Groups 1 and 3, $p < 0.00$. (C) (bottom right) Grip strength (lb) of mice ($n = 10$) of IDPN treated Groups 2 and 3 as compared to control Group 1. Data represents percent change from the control Group during 9 1/2 weeks of IDPN treatment.

0.1159 lb ± 0.009, $p < 0.00$) was observed as compared to age matched control Group 1 (0.2461 lb ± 0.032) (Fig. 1A and B). The normal age related increase in grip strength in the control Group 1 was 92.5% from the start to the end of 9 1/2 weeks (Fig. 1B). In contrast, IDPN treated Groups 2 and 3 showed 13.9% and 15.5% decrease, respectively, manifesting a neurotoxin related inhibition of normal grip strength at the end of the treatment period when the mice in each group attained the age of 14 weeks. An overall age-matched comparison showed a sequential decline in an age related grip strength at the end of 9 1/2 weeks of IDPN treatment that were 86% in Group 2 and 84% in Group 3 as compared to a concomitant increase of 192% in control Group 1 (Fig. 1A). A significant decrease in grip strength in experimental groups as compared to control group was caused by IDPN between the four and fourteen weeks of age (Fig. 1C).

Effect of EMF exposure on forelimb grip strength of IDPN treated mice Group 2

Prior to EMF exposure the forelimb grip strength values in IDPN treated mice (Groups 2-0.1147 lb ± 0.08, Group 3-0.1159 lb ± 0.009) showed no significant difference ($p < 0.7$). The EMF exposure to IDPN treated Group 2 resulted in a steep rise in grip strength (to 0.2030 lb ± 0.010) until the fourth week. Thereafter, it increased steadily up to the termination of EMF exposure at 8 1/2 weeks (0.2264 lb ± 0.013) and was close to control Group 1 values (0.2588 lb ± 0.037) (Fig. 2A). A statistically significant recovery in grip strength occurred as early as 8 weeks of EMF exposure with a minimal difference ($p < 0.05$) from the control group (Fig. 2B). The grip strength increase of 97.3% in Group 2 from the start to the end point of EMF exposure (Fig. 2B), and one week later a 87% improvement as compared to control Group1 indicated a noteworthy recovery from motor-neuropathy (Fig. 2C). However, in the absence of EMF exposure, IDPN treated Group 3 had a significantly low grip strength as compared to both EMF exposed Group 2 ($p < 0.01$) and the control Group 1 ($p < 0.00$) (Fig. 2B). The lack of EMF exposure in Group 3 that remained at the initial four weeks level in grip strength indicated only a 27.5% age related increase in grip strength between fourteen to twenty four weeks of age (Fig. 2B). The neurotoxin effect persisted as indicated by 56% lower grip strength in Group 3 as compared to control Group

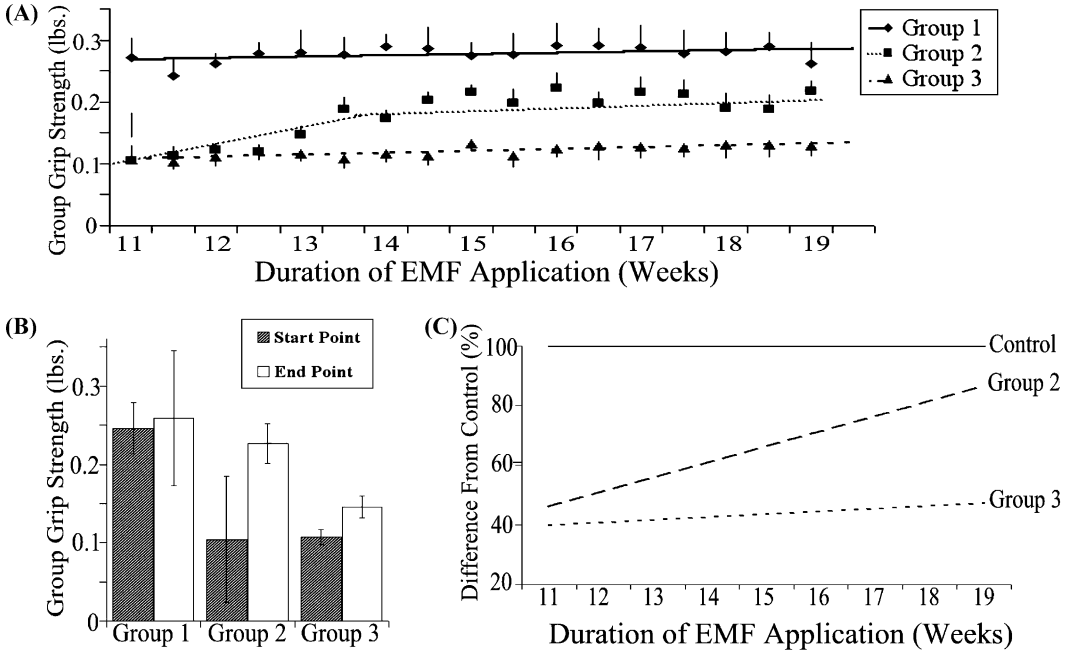

Fig. 2 (A) (Top) Grip strength (lb) in mice ($n = 10$) of IDPN treated Group 2 receiving EMF application for 8 1/2 weeks as compared to Group 3 with no EMF application and the control Group 1 (mean ± SD). (B) (bottom left) Grip strength (lb) in mice ($n = 10$) of Group 2 at the start and end points of 8 1/2 weeks of EMF application as compared to Group 3 with no EMF application and the control Group 1 (mean ± SD). Percent change in grip strength between the start and end points during 8 1/2 weeks with statistical comparison between the groups. Change of grip strength between start and end of EMF exposure period: Group 1: 5.2% increase, Group 2: 97.3% increase, Group 3: 35% increase. Pre-EMF exposure group difference: Group 1 and 2, $p < 0.00$, Group 1 and 3, $p < 0.00$. Group 2 and 3, $p < 0.7$. Post-EMF exposure group difference: Group 1 and 2, $p < 0.05$, Group 1 and 3, $p < 0.00$, Group 2 and 3, $p < 0.01$. (C) (Bottom Right) Grip strength (lb) in mice ($n = 10$) of Group 2 receiving EMF application, Group 3 with no EMF application and control Group 1. Data represent percent change from the control Group 1 during 8 1/2 weeks.

(Fig. 1C). In control Group 1 on the 19th week of the experiment, the normal age related increase in grip strength was significantly overridden by IDPN's effect in Group 3. However, as mice in each group reached 24 weeks of age at the termination of EMF application a consistent increase in grip strength was observed in EMF exposed Group 2 as the level approached that of control Group 1.

At the 19th week of the experiment following the termination of EMF exposure, a weekly recording of grip strength up to the 7th week and continued on the 16th and 27th week showed that the recovery was sustained in Group 2 (Fig. 3A and B). The grip strength recorded on the last day of EMF exposure at the 19th week of the experiment (Fig. 2A and C) was maintained at an 82% recovery level in Group 2 until the end of experimental observation on the 27th week, when mice reached an age of 52 weeks (Fig. 3B).

Electronmicrograph of radial nerves cross sections of control and experimental groups

The cross sections of radial nerves from control Group 1 (Fig. 4) showed a distinct profile of its subcellular components such as Schwann cells with conspicuous mitochondria and Golgi bodies and a normal alignment of the axonal membrane with the myelin sheath in a lamellar arrangement (Fig. 4A). An even distribution of neurofilaments and microtubules (Fig. 4C) were indicative of a normal morphology of the axon and furthermore, mitochondria exhibited a condensed conformation with increased matrix density and distinct outer and inner membranes, the latter with cristae (Fig. 4A and C). In addition, mitochondria showing binary fission (Fig. 4B) were a sign of normal functional morphology of the axon.

However, a significant deviation from the normal subcellular structure was apparent in nerve cross sections of IDPN treated Group 3 mice not treated with EMF

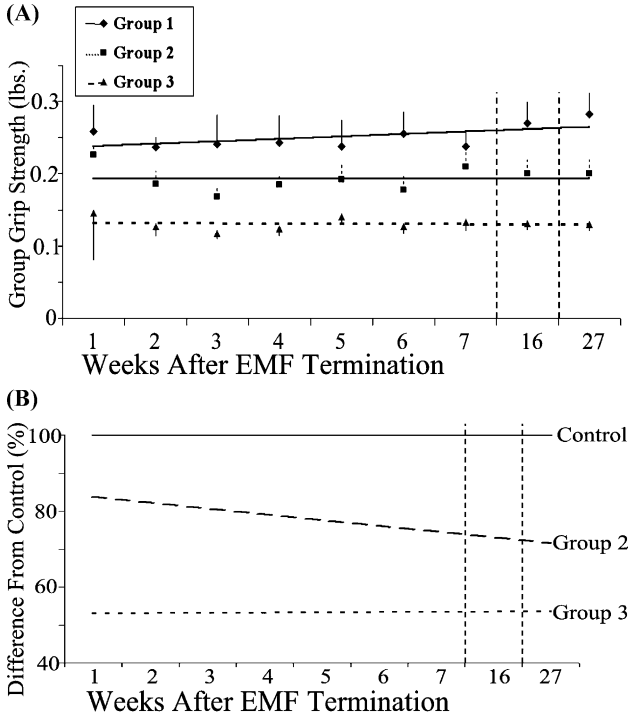

Fig. 3 (A) (Top) Grip strength (lb) in mice ($n=9$) of Group 2 after EMF application up to 27th week of observation as compared to Group 3 with no EMF application and the control Group 1 (mean $\pm$ SD). (B) (bottom) Grip strength (lb) in mice ($n=9$) of Group 2 after EMF application up to 27th week of observation as compared to Group 3 with no EMF application. Data represent percent change from the control Group 1.

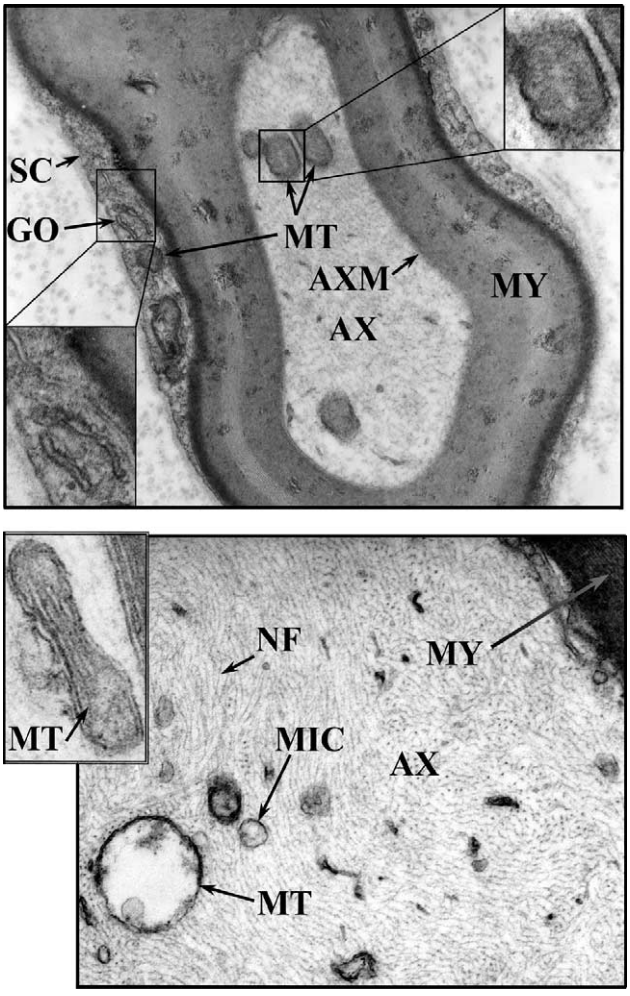

Fig. 4 Electron micrograph (EM) of cross sections of radial nerve of mice from control Group 1, indicating Axon (AX), Axonal membrane (AXM), Golgi bodies (GO), Microtubule (MIC), Mitochondria (MT), Myelin sheath (MY), Neurofilament (NF), Schwann cells (SC). (A) (Top) GO, MT, (B) (bottom left) MT binary fission, (C) (bottom) NF. EM Magnification 19,000×. Scale bar = 1 μm.

(Fig. 5). Myelin sheath with distorted lamellae was separated from axonal membrane indicating nerve degeneration due to damage to the myelin structure. Schwann cells exhibited inconspicuous mitochondria (Fig. 5A and B). The neurofilaments and microtubules were sparse and of uneven distribution. Mitochondria were present in an orthodox state of conformation (Fig. 5B) indicating decreased matrix density, indistinguishable double membranes and few cristae suggesting a metabolically inactive state. It was evident that an impairment of the normal cellular structure of the nerve, concomitant with the loss of forelimb grip strength in IDPN treated Group 3 mice, appeared to be related.

The subcellular morphology of the nerves following EMF exposure to IDPN treated mice in Group 2 (Fig. 6) was restored and was similar to that of control Group 1 (Fig. 4). The Schwann cells with distinct mitochondria and Golgi bodies (Fig. 6B and C) as well as lamellar myelin sheath (Fig. 6A) were indicative of a normal state of the axon. The remyelination of the axon and consequent grip strength recovery in Group 2 indicated a biological effect of EMF on Schwann cells, which are responsible for the formation of myelin sheath. Moreover, condensed state of mitochondria as well as few undergoing binary fission indicated metabolic activity necessary to restoration of nerve function.

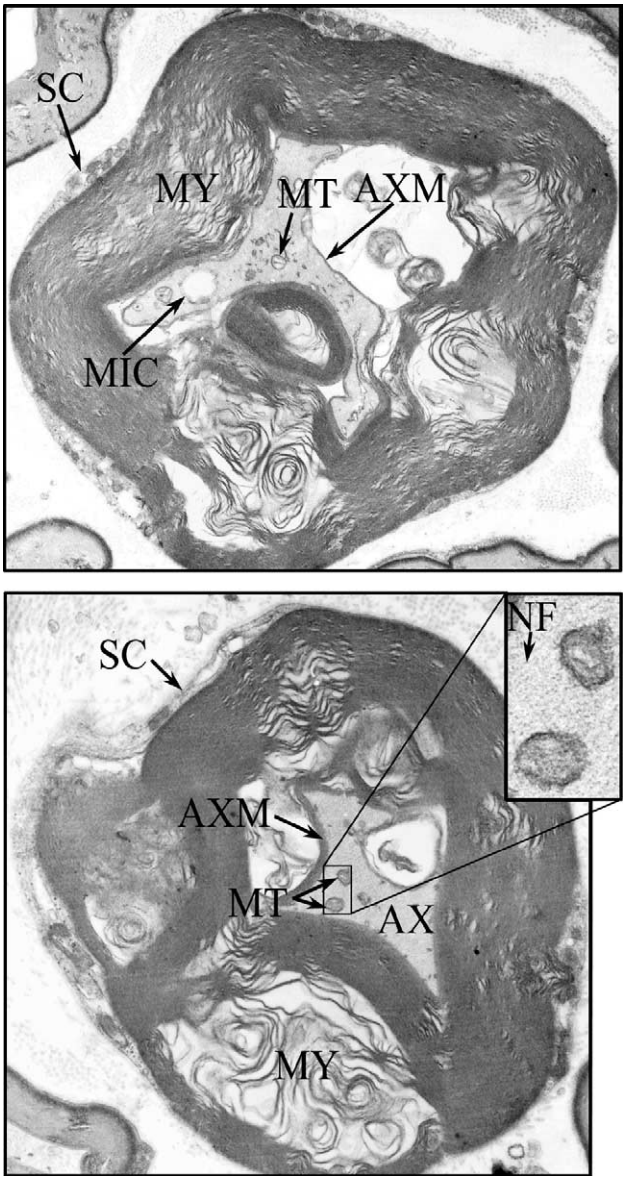

Fig. 5 Electron micrograph (EM) of cross sections of radial nerve of mice from IDPN treated Group 3 unexposed to EMF indicating Axon (AX), Axonal membrane (AXM), Microtubule (MIC), Mitochondria (MT), Myelin sheath (MY), Neurofilament (NF), Schwann cells (SC). (A) (Top) MY, AXM, (B) (bottom) MY, AXM, MT, NF. EM Magnification 10,000×. Scale bar = 1 μm.

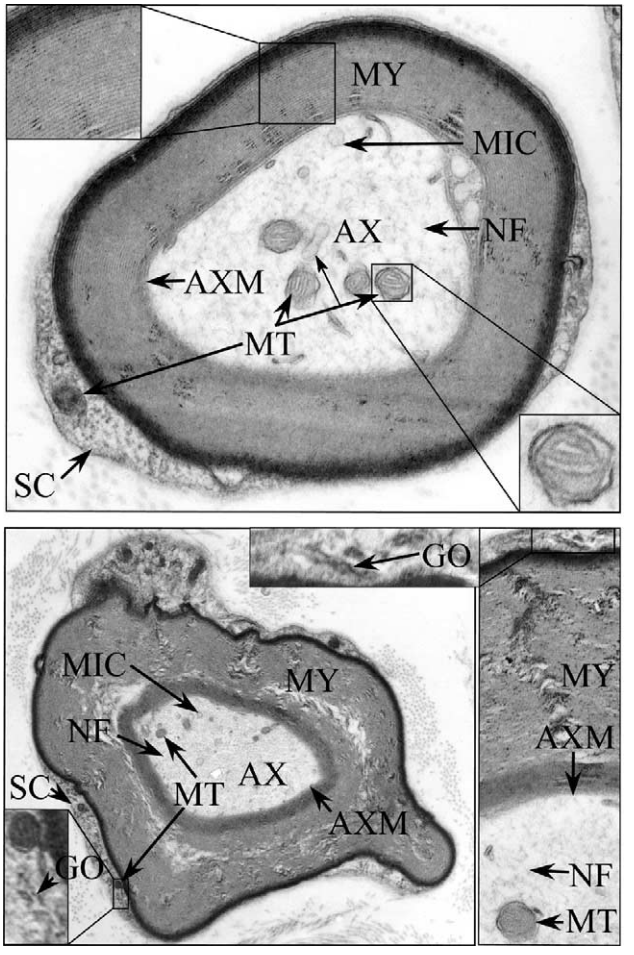

Fig. 6 Electron micrographs (EM) of cross sections of radial nerve of mice from IDPN treated Group 2 exposed to EMF, indicating Axon (AX), Axonal membrane (AXM), Golgi bodies (GO), Microtubule (MIC), Mitochondria (MT), Myelin sheath (MY), Neurofilament (NF), Schwann cells (SC). (A) (Top) MT, MY, AXM, NF, MIC, (B) (bottom left) GO, MIC, (C) (Bottom Right) GO, NF, MY, MT. EM Magnification (A and B) 19,000×, (C) 4800×. Scale bar = 1 μm.

Discussion

The development of partial motorneuropathy in mice by the administration of IDPN, a neurotoxin that induced nerve degeneration provided an animal model to study the *in vivo* effectiveness of EMF on the changes in forelimb grip strength and radial nerve ultrastructure. The gradual loss in the forelimb grip test values (Fig. 1A and B) in IDPN treated mice as measured by force gauge meter was indicative of a change in the nerve conduction in the forelimb. This was substantiated by an uneven distribution of axonal neurofilaments (Fig. 5B), which normally determine the growth of axonal diameter and slow axonal transport for impulse conduction. Further the uneven dispersion of the microtubules (Fig. 5B) affecting its function in normal longitudinal growth and in fast axonal transport verified the state of nerve degeneration. In another motorneuropathy model (65), a slow conduction velocity due to axonal atrophy was detected by electromyography in IDPN treated rats, and was attributed to the dilation of axon having a thin myelin sheath in the proximal part of the spinal cord ventral root but without any segmental demyelination of the tibial nerve. Further studies indicated (66) that the migration of the slow component of neurofilament proteins was arrested along the axon of IDPN treated rat nerves. Moreover, a segregation of the neurofilaments towards the periphery, microtubules at the center of the axon and a disassembly in cross-links of microtubule associated proteins (MAP) with transport vesicles were shown (67) in nerve samples of IDPN treated rats by deep-etch electronmicroscopy. It may be concluded that a lack of proper assembly of neurofilaments and microtubules impacted the grip strength in mice by preventing transport of major nerve molecules for neuromuscular function. Moreover the myelin sheath, a vital component in the conduction of nerve impulse was first seen damaged in the radial nerve of mice due to IDPN toxicity (Fig. 5A and B). Demyelination of axons and the severity of lesions associated with loss of conduction of nerve impulse and grip strength in mice as observed in this study has been defined as neurapraxia (68).

In IDPN treated Group 3 mice, most of the mitochondria appeared to be in an orthodox state of conformation (Fig. 5B). The condensed to orthodox state transformation in mitochondria occurred in conditions when ADP is deficient. Reversal to a condensed state corresponded with the oxidative phosphorylation reaction and ATP synthesis, dependent upon ADP and Proton permeability of the mitochondria. It is suggested that the orthodox state of mitochondria in IDPN treated mice was indicative of a reduced metabolic activity in nerves. The condensed state of mitochondria as observed in IDPN treated mice in Group 2 after EMF exposure (Fig. 6A) indicated a metabolically active condition in axons and Schwann cells.

In a previous study, excised pieces of sciatic nerves of mice in-vitro culture medium maintained a normal myelin sheath structure during EMF exposure (30). This could be attributed to Schwann cell activity along the axons, which is known to play a critical role (69) in the myelination of nerve fibers after being disconnected from central nervous system (CNS) neurons, a source of neurotropin for nerve growth. Schwann cells produce a number of polypeptide nerve growth factors (NGF) for their own development and propagation (70,71). It has also been known that nerve injury induces an increased output of NGF from Schwann cells (72). These studies support an autonomous role of Schwann cells in maintaining metabolic functions in the proximity of axons (73,74), by releasing NGF for myelin formation and acting as an NGF receptor. In the present in vivo study, two sources of NGF were apparently available to the intact nerve fibers, one from CNS neurons and the other from Schwann cells. EMF exposure may have enhanced the action of the Schwann cells in IDPN treated Group 2 mice. These Schwann cells (Fig. 6B and C) indicated distinct Golgi bodies (GO) that are the source of NGF secretion resulting in the remyelination of axons. A link between EMF leading to normal Schwann cell function indicated that a non-neuronal control in the regeneration and growth of peripheral nerve fibers are definitely possible.

The restoration of neurotoxin impaired subcellular structure of radial nerves of mice in Group 2 treated with EMF exposure is supported by the reappearance of mitochondria in a condensed state both in axons and Schwann cells. The physiological state of mitochondria as observed indicated its normal membrane permeability and a recovery of ATP synthesis essential for nerve growth and repair. Other ATP dependent processes such as the organization of neurofilaments and microtubules for axonal slow and fast transport systems were also restored. ADEY (8,61,62) showed that the molecular signaling across an axonal membrane may be extensively modified by a low energy level of an applied electromagnetic field and is attained by cooperative amplification that restored cellular function. In the present study, molecules critical in nerve conduction and metabolic activity (Table 1) were significantly affected during EMF exposure. Therefore, the EMF of physiological ranges may have created an additive effect on the recovery of grip strength in mice. Furthermore, a distinct correlation with simultaneous restoration of the subcellular morphology of nerves supported that nerve metabolic processes were initiated and sustained.

In this study, the effectiveness of low intensities and frequencies of EMF was significantly demonstrated in vivo by the restoration of subcellular nerve structure

and by grip strength recovery sustained up to the 27th week of observation in mice with motorneuropathy. It is suggested that the loss of nerve structure and function may result in a change in the inherent transmembrane potential. This potential could be manipulated by an externally applied EMF, which restored the intrinsic charge distribution of molecules vital for nerve conduction and metabolism. A role of EMF in recovery from nerve injury, spinal cord traumas, and peripheral neuropathies may be postulated on the basis of selectively modulating neurotropins and their receptors. Further dose–response studies are required to determine a therapeutic model for EMF application in the treatment of nerve dysfunctions.

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REFERENCES

1. Nordenstrom B. In: *Biologically Closed Electric Circuits*. Stockholm: Nordic Medica, 1983: 152–172.
2. Nordenstrom B. The paradigm of biologically closed electric circuits (BCEC systems). Presidential address. *European Journal of Surgery* 1994; **574**: 7–23.
3. Jacobson J. I. *The Secret of Life*. New York: Philosophical Library, 1983.
4. Jacobson J. I. A testable theoretical model for the mechanism of magnetotherapy. *J Italian Med Assoc Pan Minerva Medica* 1987; **29**(4): 263–270.
5. Jacobson J. I. Jacobson Resonance is the basis from which to evaluate potential hazard and therapeutic benefit from extrinsic magnetic fields. *Pan Minerva Medica* 1993; **35**: 138–148.
6. Jacobson J. I. Speculations on the influence of electromagnetism on genomic and associated structures. *Int Med Res* 1996; **24**(1): 1–12.
7. Jacobson J. I., Yamanashi W. S. A possible physical mechanism in the treatment of neurologic disorders with externally applied picoTesla magnetic fields. *Phys Chem Phys Med NMR* 1996; **26**(4): 287–297.
8. Adey W. R. Whispering between cells: Electromagnetic fields and regulatory mechanisms in tissue. *Frontier Perspectives* 1993; **3**(2): 21–25.
9. Liboff A. R. Cyclotron resonance in membrane transport. In: A. Chiabarera, P. Niccolini, H. Schwan (eds). *Interactions Between EM fields and Cells*. New York: Plenum, 1985: 281–296.
10. Jacobson J. I., Yamanashi W. S., Saxena A., Brown B., Parekh P., Shin D., Saxena B. Effect of magnetic fields on damaged mice sciatic nerves. *J Administrative Radiol* 2000; **19**(34): 22–25.
11. Kaczmarek L. K., Adey W. R. The efflux of $45Ca^{2+}$ and 3H-γ-amniobutyric acid from cat cerebral cortex. *Brain Res* 1973; **63**: 331–342.
12. Jacobson J. I., Yamanashi W. S. An initial physical mechanism in the treatment of neurologic disorders with externally applied picoTesla magnetic fields. *Neurol Res* 1995; **17**: 144–148.
13. F. O. Schmitt, D. M. Shneider, D. M. Crothers (eds). *Functional Linkage in Biomolecular Systems*. New York: Raven, 1975.
14. Lowden P. O. Proton tunneling in DNA and its biological implications. *Rev Med Phys* 1963; **35**: 724–732.
15. Adey WR. Physiological signaling across cell membranes and cooperative influences of extremely low frequency EM fields in biological coherence and response to external stimuli. Frohlich H, editor. New York: Springer, 1988: 148–170.
16. Clegg J. S. Properties and metabolism of the aqueous cytoplasm and its boundaries. *Am J Phisol* 1984; **246**: R51–R133.
17. DelGiudice E., Doglia S., Milani M. Self focusing and ponderomotive forces of coherent electric waves: a mechanism for cytoskeleton formation and dynamics. In: H. Frohlich, F. Kremer (eds). *Coherent Excitations in Biological Systems*. Berlin: Springer, 1983: 123–127.
18. Murzin A. G., Finkelstein A. V. *J Mol Biol* 1988; **204**: 749–770.
19. Anninos P. A., Tsagas N., Sandyk R. Magnetic stimulation in the treatment of partial seizures. *Int J Neurosci* 1991; **60**: 141–171.
20. Sandyk R. Magnetic fields in the therapy of Parkinsonism. *Int J Neurosci* 1992; **66**: 209–235.
21. Jacobson J. I. A brief review of picoTesla range magnetotherapies. Estratto Da Gazzetta Medico Italiana-Archivo Per I.E. *Sci Med* 1998; **157**(2): 37–41, Ediozioni Minerva Medica, Torino.
22. Jacobson J. I. Jacobson Resonance: the quantum-mechanical basis for a novel radiological approach to treating cancer and AIDS. *Frontier Perspectives (Temple University)* 1996; **6**(1): 17–27.
23. Jacobson J. I. A look at the possible mechanism and potential of magnetotherapy. *J Theoret Biol* 1991; **148**: 97–120.
24. Jacobson J. I. Exploring the potential of magneto-recrystallization of genes and associated structures with respect to nerve regeneration and cancer. *Int J Neurosci* 1992; **64**: 153–165.
25. Jacobson J. I. Oncogenes and magnetic resonance energies unified algebraically. *Pan Minerva Medica* 1987; **29**: 97–104.
26. Jacobson J. I. A magnetic approach to AIDS. *Pan Minerva Medica (Quart J Eur Med)* 1995; **37**(1): 22–27.
27. Einstein A. In: *Ideas and Opinions*. New York: Bonanza Books, Copyrighted by Crown Publishers, 1954: 92–93. 372–377.
28. Einstein A., Lorentz H., Wekyl H., Minkowski H. In: *The Principle of Relativity*. New York: Dover, 1952,: 143–198.
29. Appelquist T., Chodos A., Freund E. Modern Kaluza-Llein theories, chapter. In: R. Candelas, S. Weinberg (eds). *Calculation of Gauge Coupling and Compact Circumferences from Self-consistent Dimensional Reduction*. New York: Addison-Wesley, 1987: 575–579.
30. Jacobson J. I., Yamanashi W., Brown B., Parekh P., Shin D., Saxena B. Effect of magnetic fields on damaged mice sciatic nerves. *Frontier Perspectives* 2000; **9**(1): 6–11.
31. Todorov A. T. et al. Electric field induced reconnection of severed axons. *Brain Res* 1992; **582**: 329–334.

32. Kern J. M. et al. Electrical stimulation of nerve regeneration in the rat: the early effects evaluated by a vibrating probe and electron microscopy. *Neuroscience* 1991; **40**: 93–97.
33. Borgens R. B., Bonhert D. M. The response of mammalian spinal axons to an applied DC voltage gradient. *Exp Neurol* 1997; **45**: 376–389.
34. Rusovan A., Kanje M. Stimulation of regeneration of the rat sciatic nerve by 50 Hz sinusoidal magnetic fields. *Exp Neurol* 1991; **112**: 312–316.
35. Pool Is there an EMF-cancer connection? *Science* 1990; **249**: 1096–1098.
36. Adey W. R. Tissue interactions with nonionizing EM fields. *Physiol Rev* 1981; **61**(2): 435–445.
37. Pierce S., Biblow C. Electromagnetic fields attract lawsuits. *Natl Law J* 1993; **8**: 20.
38. Goodman R., Henderson A. Transcription in cells exposed to extremely low frequency EM fields: A review. *Bioelectrochem Bioenerget* 1991; **25**: 325–355.
39. Goodman R., Henderson A. Exposure of human cells to low frequency EM fields results in quantitative changes in transcripts. *Bio Chem – Bio Physica Acta* 1989; **1009**: 216–220.
40. Decker C. ELF-zapped genes speed DNA transcriptions. *Sci News* 1990: 229.
41. Zanakis M, Politis M. Facilitated regeneration with the rat peripheral nervous system using applied electric fields. J. Trauma 1998; **28**(*9*): 1–6.
42. Zanakis M., Politis M. Treatment of rat hippocampus with a locally applied electric field. *Exp Brain Res* 1988; **71**: 223–226.
43. Bistolfi F. A hydrogen-harps model for intracellular communication and its implications for the second genetic code. *Pan Minerva Medica* 1990; **32**(1): 4–9.
44. Einstein A. In: *Out of My Later Years*. New York: Philosophical Library, 1956: 93.
45. Bistolfi F. Biostructures and radiation order disorder. *Edizioni Minerva Medica Torino* 1991: 27, 53, 67, 73, 91, 103.
46. Cope F. W. Discontinuous magnetic field effects (Barkhausen noise) in nucleic acids is evidence for room temperature organic superconduction. *Physiol Chem Phys* 1978; **10**: 233–246.
47. Cohen D. Detection of the brain's electrical activity with a superconducting magnetometer. *Science* 1972; **175**: 664.
48. Sandyk R. Successful treatment of multiple sclerosis with magnetic fields. *Int J Neurosci* 1992; **66**: 237–250.
49. Anninos P. A., Jacobson J. I., Tsagas N., Adamopoulos A. A spatiotemporal stationarity of epileptic focal activity evaluated by analyzing magnetoencephalographic (MEG) data and the theoretical implications. *Pan Minerva Medica (Ital Med Assoc)* 1997; **39**(3): 189–201.
50. Nordenstrom B. Circuits electriques biologiquement fermés, leur signification dans les ransformations structurales dans le cancer du sein. Presented at the1st International Course of Radiodiagnosis of the Breast. Montpelier, France, Mar. 24–27, 1981.
51. Bistolfi F. A new approach to the interaction between ionizing radiation and biostructure: the dual compartment interaction model. *Radiol Med* 1991; **81**(Suppl. 1): 99–108.
52. Bistolfi F, Olzi E. Prospettive di concentrazione magnetotassica di elementi paramagnetici in terapi oncologica. Il Progresso Tecnologico in Radioterapia Oncologia, Varese 28–29, 1984. Abstracts Issue: 66–67.
53. Feychting M., Ahlbom A. Magnetic fields and cancer in children residing near Swedish high voltage power lines. Institutet for Miljomedicin, Karolinska Institute. Stockholm, Sweden. *Am J Epidemiol* 1993; **7**: 467–481.
54. R. G. Stevens, L. E. Anderson (eds). *Extremely Low Frequency Electromagnetic Fields: The Question of Cancer*. Columbus, OH: Battelle Press, 1990: 211–229.
55. Pool M. Is there an EMF-cancer connection?. *Science* 1990; **249**: 1096–1098.
56. Jacobson J. I., Gorman R., Chaviano F., Yamanashi W. S., Grinberg I., Dayton M., Haltiwanger S., Saxena B. B., Walters B., Clayton L., Lamberth J. PicoTesla range magnetic fields tested in four site double blind clinical study for treatment of osteoarthritic knees. *Gazzetta Medica Italiana-Archivio Per Le Scienze Mediche* 2001; **160**: 1–20.
57. Rakhimov R. Resonance therapy by means of narrow - spectrum ceramic infrared emitters. The Endocrine Society, 82nd Annual Meeting Toronto, Canada. Abstract Mo. 353:93, 2000.
58. Goodman R., Henderson A. S. Exposure of salivary gland cells to low frequency electromagnetic fields alters polypeptide synthesis. *Proc Natl Acad Sci USA* 1988; **85**: 3928–3932.
59. Yamaguchi H., Hosokawa K., Soda A., Mizamoto H., Kinouchi Y. Effects of seven months of exposure to a static 0.2 T magnetic field on growth and glycolytic activity of human gingival fibroblast. *Biochem Biophys Acta* 1993; **1156**: 302–306.
60. Blank M., Soo L. The Na, K-ATPase as a model for electromagnetic field effects on cells. *Bioelectrochem Bioenerget* 1993; **30**: 85–92.
61. Adey W. R. The sequence of cell membrane transductive coupling to intracellular enzyme systems. *Bioelectrochem Bioenerget* 1986; **15**: 447–456.
62. Adey W. R. In: *Interaction Mechanisms of Low-Level Electromagnetic Fields in Living Systems*. New York: Oxford University Press, 1992: 47–77.
63. Kitahara J., Maki T., Torh H. K. Effect of dietary supplementation with branched-chain amino acids on spontaneous motor activity and muscle function in β-β′-iminodipropionitrile-treated rats: A model for motorneuropathy. *Physiol Behav* 1997; **62**(3): 453–462.
64. Jacobson J. I. $MC^2 =$ BVL Coulomb Gravitational and electromagnetic interaction energies in dual resonance. *Ind J Theor Phys* 1986; **34**(8): 231–239.
65. Höfinger E. P., Le Quesne M., Gajree T. Conduction velocity in nerve fibres with axonal atrophy due to chronic β, β'- Iminodiproprionitrile (IDPN). *J Neurol Sci* 1982; **53**: 159–167.
66. Griffin J. W., Hoffman P. N., Clark A. W., Carroll P. T., Price D. L. Slow axonal transport of neurofilament proteins :Impairment by β,β′-iminodipropionitrile administration. *Science* 1978; **202**: 633–635.
67. Hirokawa N., Bloom G. S., Vallee R. B. Cytoskeletal architecture and immunocytochemical localization of microtubule-associated proteins in regions of axons associated with rapid axonal transport: The β,β′-iminodipropionitrile- intoxicated axon as a model system. *J Cell Biol* 1985; **101**: 227–239.
68. Seddon H. J. Classification of nerve injuries. *Br Med J* 1942; **11**: 237–239.
69. Gould R. M., Jessen K. R., Mirsky R., Tennekoon G. The cell of Schwann: An update. In: R. E. Martenson (ed). *Myelin:*

Biology and Chemistry. Boca Raton, FL: CRC Press, 1992: 123–171.
70. Dong Z., Brennan A., Liu N., Yarden Y., Lefkowitz G., Mirsky R., Jessen K. R. Neu differentiation factor is a neuron-glia signal and regulates survival, proliferation and maturation of rat Schwann cell precursors. *Neuron* 1995; **15**: 585–596.
71. Raabe T. D., Francis A., de Vries G. H. Neuregulins in glial cells. *Neurochem Res* 1998; **23**: 311–318.
72. Heumann R. S., Korsching C., Bandtlow, Thoenen H. Changes of nerve growth factor synthesis in non-neuronal cells in response to sciatic nerve transection. *J Cell Biol* 1987; **104**: 1623–1631.
73. Acheson A., Barker P. A., Alderson R. F., Miller F. D., Murphy R. A. Detection of brain-derived neurotrophic factor-like activity in fibroblasts and Schwann cells: inhibition by antibodies to NGF. *Neuron* 1991; **7**: 265–275.
74. Althaus H. H., Richter-Landsberg C. Glial cells as targets and producers of neurotropins. *Int Rev Cytol* 2000; **197**: 203–277.
75. Wever R. The Circadian multi-oscillatory system of man. *Int J Chronobiol* 1975; **3**: 19–55.
76. Galvalas-Medici R., Day-Magdaleno S. R. Extremely low frequency weak electric fields affect schedule – controlled behavior of monkeys. *Nature* 1976; **261**: 256–258.
77. Kalmijn AJ. The electric sense of sharks and rays. J Exp Biol X971; **55**: 371–383.
78. Turing A. M. The Chemical Basis of Morphogenesis. *Philos Trans R Soc Lond B* 1952; **237**: 37–72.
79. Othmer H. G., Scriven L. E. Nonlinear aspects of dynamic pattern in cellular networks. *J Theor Biol* 1974; **43**: 83–112.
80. Katchalsky A., Curran P. F. *Non Equilibrium Thermodynamics in Biophysics*. Cambridge MA: Harvard University Press, 1965.
81. F. O. Schmitt, D. M. Shneider, D. M. Crothers (eds). *Functional Linkage in Biomolecular Systems*. New York, NY: Raven, 1975.
82. Wyman J., Allen D. W. The problem of the Leme Interactions in Hemoglobin and the basis of the Bohr effect. *J Polymer Sci* 1951; **7**: 491–518.
83. Sandyk R. Successful treatment of Multiple Sclerosis with magnetic fields. *Int J Neurosci* 1992; **66**: 250–273.
84. Jacobson J. I., Yamanashi W. S. A possible, physical mechanism in the treatment of neurologic disorders with externally applied picoTesla magnetic fields. *Physiol Chem Phys Med NMR* 1994; **26**: 287–297.
85. Willey R. L. *Microtechniques: A Laboratory Guide*. New York, NY: Macmillan, 1971.