Uses of Magnetic Fields for Health Applications

Subjects: Biophysics
Contributor: David A. Hart

Early life on Earth evolved in the contexts of temperature, available elements, and molecules (including water), as well as the biophysical boundary conditions of the planet. The latter include gravity (1 g), exogenous and endogenous radiation from particles from beyond Earth and radioactive elements on Earth, and magnetic fields due to the planet's magnetic field and local concentrations of molecules such as iron. Humans and other animals, plants, and microorganisms have been exposed to a variety of magnetic fields other than the geomagnetic field of Earth and deposits of ferro materials. Magnetic fields, static or electromagnetic, have been used in attempts to improve outcomes for the repair of a variety of tissues.

geomagnetic field | magnetic fields | tissue | brain | wound healing

1. Introduction

Life on Earth evolved slowly from simple single-cell entities that could eventually reproduce themselves using information storage molecules such as DNA, initially as prokaryotes, and eventually as eukaryotes with subcellular organelles including mitochondria, such cells adapted to a variety of environmental conditions (i.e., deep ocean vents, fresh water, cold to hot water). Interestingly, most life consists primarily of water.

In addition to securing the ability to form a plasma membrane and the machinery to perform essential functions, primitive cells needed to develop these abilities within the context of the physical and biophysical boundary conditions of Earth. These include background radiation and radiation from space that was not deflected by the geomagnetic field of the planet, the 1 g gravity of the planet, and the actual geomagnetic field plus any local magnetic influences. Thus, successful early life must have evolved mechanisms to negate such influences or evolved adaptations to embrace their influences.

As life likely evolved initially in oceans, lakes, or other water environments, perhaps initially boundary conditions such as the 1 g gravity were sensed, but further adaptations were required when complex life emerged onto land and mobility and navigation were advantageous. However, the influence of the geomagnetic field would have been felt in early life forms, either with regard to incorporating elements such as iron ions into essential processes or potentially in other as yet unknown defined manners. The commitment to an information-containing molecule such as DNA being central to reproduction fidelity is also an interesting choice as it can be sensitive to radiation damage and induction of mutations. However, early in evolution, this sensitivity could have been used advantageously to use mutations to adapt to a changing biological and physical environment. Mutations could arise from a lack of fidelity in copying the DNA and/or radiation-induced effects. As life becomes more complex and multi-cellular with differentiated functions, it is also likely that methods to minimize such influences would develop to decrease the likelihood of developing adverse situations that would compromise organism integrity. These latter could include tumor suppressor genes, DNA repair mechanisms, and controlled cell death.

While the 1 g gravity of Earth would have been felt by organisms and resulted in settling to the bottom of a lake or near a vent in the ocean, organisms could have resisted this effect via the movement of the water or by attaching themselves to something in shallow water and nutrients could have come to them via water movement. The real impact of the 1 g gravity environment would likely have been felt when multi-cellular organisms emerged to live on land, and the advantage of mobility and navigation against ground reaction forces required the evolution of new adaptations. Thus, the development of legs for quadrupedal movement and legs and arms for bipedal mobility required the evolution of effective adaptations and integration with visual or other sensors. Also of interest in this regard are species that lived on land and developed legs but then returned to the marine environment (i.e., whales and other marine mammals). The cardiovascular system of complex lifeforms living on land also required adaptations to function in the 1 g environment. As all tissues except perhaps articular cartilage are vascularized and innervated, these adaptations would affect all organ systems.

As evolution could not have predicted space flight and exposure to microgravity, it is interesting that the atrophy of mechanically loaded tissues such as bone and muscles is rapidly evident after leaving Earth and living at LEO (discussed in [1]). In addition, cardiovascular effects are also very evident after exposure to microgravity. Interestingly, even prolonged bedrest on Earth leads to loss of bone and muscle and cardiovascular changes, so such tissues have evolved a “use it or lose it” paradigm even when still under the influence of a 1 g gravity environment on Earth (discussed in [1][2]).

Another major boundary condition, the geomagnetic field, certainly “protects” life forms from the negative influence of solar radiation (discussed in [3]). Many forms of exogenous radiation originating from the sun or other cosmic sources (i.e., pulsars, black holes, supernovas] can be deflected by this magnetic field (discussed in [3]), thus protecting the DNA from mutational events or resulting in cell death. For example, it has been reported to enhance radiation resistance by promoting DNA repair processes in cells [4]. From reading the literature, this attribute is the main influence of the geomagnetic field on life. The real question then becomes, “is it the only role?” and if so, why and how did life forms develop systems that use electrical signaling with concomitant magnetic field generation within a powerful magnetic field? Such an environment may have led to the development of a bioelectric code early in the evolution of simple and then more complex life forms [5], and such a code would also have an electromagnetic component. Thus, such a system may respond to exogenous magnetic fields as well [6]. It would be intuitive to conclude that commitment to such systems, such as the brain and neural systems, as well as the heart and cardiovascular system, could have evolved approaches to either negate the geomagnetic field or embrace it. Furthermore, as the distribution of elements on Earth that could lead to local magnetic fields is not uniform (i.e., large deposits of iron-containing hematite and taconite non-uniformly concentrated in various locals), the evolved adaptations to the geomagnetic field must account for the exposure to such local concentrations or suffer the consequences.

Humans and other animals, plants, and microorganisms have been exposed to a variety of magnetic fields other than the geomagnetic field of Earth and deposits of ferro materials (discussed in [7]). In addition, magnetic fields, static or electromagnetic, have been used for decades in attempts to improve outcomes for the repair of a variety of tissues (reviewed in [8][9][10][11][12][13]). The studies used magnetic fields of varying frequencies and intensities and employed both patient and preclinical models. However, the magnetic fields used in the studies were often variable, and it is sometimes difficult to compare studies. Magnetic fields have also been used to study cells [14] and processes such as development [15].

2. The Musculoskeletal System (MSK)

Magnetic fields have been used to influence the healing of a variety of tissues of the MSK system. These include soft tissues such as ligaments, tendons, cartilage, and menisci, as well as bone, and the studies have spanned several decades [16].

Ligament and Tendon Healing: Using a solid core electromagnet, Frank et al. [17] reported that exposure to the field following injury to the rabbit medial collateral ligament led to improved mechanical and biological healing parameters over 6 weeks. Subsequently, Lin et al. [18] reported that 2, 10, and 50 gauss (G) pulsing electromagnetic fields (PEMFs) during early healing of surgically induced defects in the rabbit patellar ligament/tendon led to improved outcomes, with 50 G yielding the best outcomes. More recently, Xu et al. [19] used exposure to a combination of static and electromagnetic fields (combined magnetic fields, CMF) to assess patella-patella tendon healing in a rabbit model. The authors assessed a variety of biomechanical and biological parameters and found that exposure to CMF led to significantly enhanced healing properties of the tissue at 16 weeks but less so at 8 weeks post-injury. Also, in a rabbit model, Hu et al. [20] demonstrated that exposure to a CMF led to an enhanced healing of the bone-tendon interface, potentially by enhancing osteogenesis. Thus, for these soft tissues and in rabbits, exposure to magnetic fields led to enhanced healing outcomes.

Meniscal and Cartilage Healing: Recently, Wang et al. [21] reported that healing of injuries to the avascular region of the menisci of male rats could be enhanced by exposure to pulsed electromagnetic fields (PEMF) over an 8-week study period. In addition, exposure to the PEMF also prevented the progression of the injury and development of osteoarthritis in the affected joints. The researchers concluded that exposure to the PEMF led to enhanced fibrocartilage production and decreased inflammation. Interestingly, studies of electromagnetic fields with patients with established osteoarthritis (OA) do not appear to have regenerative effects on tissues but may reduce pain for some patients [22][23]. Whether this effect on pain is due to an effect on inflammatory processes in OA or some other mechanism remains to be determined by future investigations.

Bone Healing: The study of exogenous magnetic fields on bone healing has had a long history (reviewed in [8][24][25][26]). Such studies have been performed on a variety of species, and investigators have used bone cells both in vivo and in vitro. In vitro studies have been used in attempts to better understand the genes influenced by PEMFs on bone cells or osteogenic precursor differentiation [27]. In guinea pigs, exposure to both static and PEMFs enhanced bone repair of mandibular osteotomies based on histology [28].

Particular emphasis on the use of magnetic fields for bone healing has been applied to promote compromised healing, such as non-unions where natural healing either is protracted or fails. However, in a recent study of PEMFs in the healing of carpal scaphoid non-unions, the PEMF did not offer any detectable benefit [29]. Similarly, EMF exposure exhibited inconclusive effects on delayed or non-union fractures of long bones in adult patients [30]. In contrast, in a small study of 29 patients, the use of a CMF protocol led to enhanced healing of a variety of non-union fractures in both male and female adults [31]. In other reviews of the literature regarding magnetic field effects on non-unions, the consensus appears to be that exposure to magnetic fields (i.e., biophysical stimulation) is an effective modality [32][33][34] and an approach that avoids some of the complications associated with surgical interventions. Whether this variation in outcomes and conclusions is due to the type of magnetic fields that are applied, when and how they are applied, or to host factors is not clear at the present time. Furthermore, it is also not clear currently how such biophysical interventions impact cells at the biochemical or molecular levels. Some reports indicate it may involve effects on iron metabolism [35], while others indicate it may be at the level of immune and inflammatory process regulation [36]. The influence could be a combination of those elements, as an emerging theme is the effect of the magnetic fields on inflammation and inflammatory processes. This conclusion would also be supported by reports indicating static magnetic fields can also influence inflammation in the liver of mice [37].

In surrogate models of bone loss in space or immobilization, namely, prolonged hindlimb elevation in rodents to remove loading of the bones, it has been reported that PEMF exposure can prevent bone loss due to hindlimb elevation in rats [38] and that exposure to a static magnetic field in addition to loading in the 1 g environment can enhance recovery of bone in mice [39]. In the rat study, the activation of the sAC/cAMP/PKA/CREB signaling pathway was involved in the prevention of bone loss [38]. In this circumstance, the rat tissues were not overtly injured but were undergoing atrophy, and thus, the results may indicate that there was an interaction between magnetism-based mechanisms and loading via gravity and the impact of ground reaction forces.

3. The Brain and Neurological Integrity

As discussed earlier, the functioning of the brain leads to the generation of electromagnetic fields that can be measured by techniques such as SQUID or magnetoencephalogram (MEG) (reviewed in [40][41]). Such techniques can be used for both fetal [42] and adult [43] brain assessment. As such, these techniques can be used to detect neurological issues during development and during aging when loss of neurological integrity can occur with some frequency. However, a limitation of techniques such as MEG is that the detection system does not penetrate deep into the brain.

3.1. Detection of Brain Injury or Diseases

Detection of mild brain injury (i.e., post-concussion syndrome) using electromagnetic approaches has been proposed [44]. MEG can also be used for localizing and characterizing epileptic events [45] and, potentially, post-traumatic stress disorders [46]. While not an “overt injury” to the brain, space flight has led to the detection of cognition-associated changes [47][48][49][50]. Some reports have questioned whether the head-down tilt bedrest, a surrogate for spaceflight, captures the true nature of spaceflight-induced cognitive changes [51]. This surrogate is performed on Earth, so the 1 g and GMF environments are still functional, but the subjects are not exposed to the ground reaction forces associated with the 1 g environment. It does, however, mimic aspects of cardiovascular changes associated with space flight (discussed in [1][52]). To effectively capture space flight-related cognitive changes, new technology for real-time assessments may be required [53].

Detection of disruptions of functional networks using MEG and fMRI have been reported in patients with dementia [54], with some characteristics associated with specific types. MEG analysis in Alzheimer's Disease [55][56][57] has revealed abnormalities, even in early disease [58][59]. In addition, some reports have discussed the potential role of magnetic fields as risk factors for the development of neurological and neurodegenerative diseases [60][61][62].

3.2. Health Benefits of Magnetic Fields on the Brain

Pulsed electromagnetic fields have been reported to positively affect microvascular perfusion and tissue oxygenation of the healthy rat brain [63]. Furthermore, the concept that electromagnetic fields could facilitate brain repair via neural stem cells has also been proposed [64] but has not yet been proven.

Interestingly, transcranial stimulation with PEMFs has been reported to positively influence depression [65][66], and potentially, transcranial magnetic stimulation may exert positive effects on post-traumatic stress disorder [67]. Furthermore, transcranial magnetic stimulation may also alleviate aspects of Alzheimer's Disease (AD) [68]. Further studies in a mouse model of AD reported that exposure to a specific frequency of electromagnetic stimulation led to improved symptoms [69]. It should be noted that these studies were performed against a background of the GMF of Earth. Thus, improvements via exposure to a specific magnetic field appeared to "correct" disease-associated defects in the functionality of the brain. While the molecular mechanisms responsible for the improvements in patients are not known, in the mouse model [69], exposure to the 900 MHZ fields led to decreased amyloid plaque deposition in specific areas of the brain of the mice.

While many aspects of studies focused on "correcting" loss of brain integrity using exposure to magnetic fields are not well described, this is an emerging field of study. There may be significant variation in outcomes depending on the frequency or intensity of the magnetic fields used for the studies. What the implications are in this regard for psychological, cognitive, or neurodegenerative conditions remains to be determined by future research activities. Recently, Dufor et al. [70] summarized the current state regarding the use of magnetic stimulation as a therapeutic approach for the repair of the compromised brain. These authors also summarized some of the mechanistic considerations for magnetic fields on the brain and brain cells, including the potential involvement of cryptochromes, reactive oxygen species, and other molecular and cellular processes.

4. Magnetic Field Effects on Wound Healing

Enhancing wound healing using magnetic fields has had a long history, with cells in vitro, preclinical models, and some patient-based studies reported [71], but most studies have used rodent models of cutaneous healing or cells in vitro [72]. In some studies, authors have used diabetic animals as wound healing in such animals is often compromised.

Using cells in vitro, exposure to a variety of static magnetic fields led to changes in cell migration via the membrane and cytoskeleton [73]. Other studies have implicated low-frequency electromagnetic fields in enhancing wound healing via anti-inflammatory mechanisms [74].

Using in vivo models, Ekici et al. [75] reported that exposure to static magnetic fields led to increased mechanical strength of dermal wounds on the backs of male rats. However, other healing parameters did not appear to be affected. As the strength of the scar tissue likely relates to the organization of the extracellular matrix, this effect of the magnetic fields may represent an effect on how well the scar tissue becomes organized. Other reports have used rats with chemically induced diabetes. Cheing et al. [76] reported that PEMFs promoted early wound healing and myofibroblast proliferation in such rats and thus enhanced wound closure. Similarly, Zhao et al. [77] reported that exposure to static magnetic fields enhanced wound closure in diabetic rats with elevated wound strength. As compromised angiogenesis in diabetic rats is one variable that may lead to impaired wound healing in diabetic rats [78][79], the magnetic fields may have improved healing by alleviating such vascular issues [11]. Also, in a rat model, exposure to PEMFs enhanced the repair following the induction of a frostbite injury [80]. Exposure to the PEMFs led to improved wound strength and accelerated growth of the deep layers following injury.

Again, these effects of magnetic fields were observed on Earth in the presence of the GMF of the planet, any local EMFs from other equipment, and any input from local deposits of Fe-containing compounds.

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