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The Effects of Electromagnetism for the Treatment of Multiple Sclerosis

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THE EFFECTS OF ELECTROMAGNETISM FOR THE TREATMENT OF MULTIPLE SCLEROSIS

by

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This Independent Study, submitted by Michele A. Morse in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

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ABSTRACT

Electromagnetic treatment is one of the highest utilized nontraditional therapeutic methods in the medical field. Scientific research has proposed that people experience improvement in the symptoms of multiple sclerosis (MS) from such treatment. This independent study is a literature review that probes into the proclaimed benefits that a low frequency electromagnetic field posses on the biological system. In order to support or negate these claims, literature and studies explaining how and why this concept is feasible is researched and presented. The review focuses on the effects of the low frequency external electromagnetic field at the cellular level and on central nervous system. The pineal gland is of utmost concern as research has indicated it as a major player in the interaction of the biological system with an external electromagnetic field

Scientific support validates physiological versus psychological effects that the application of an external electromagnetic field implies. The actual mechanisms of action with the biological system remain in hypothetical terms, therefore further studies are needed and continue on this topic. Controversy is high among some of the claimed effects of an electromagnetic field. Scientific research is certainly present supporting electromagnetic therapy as a treatment option for the symptoms of MS. However, this is not to say that magnetic therapy is beneficial for all diagnosis. In order for the person to benefit from magnetic therapy the condition must be affected by alterations in the functioning of the cell, cell membrane, transport and signaling system, ionic changes, hormonal changes, alterations in neurotransmitter substance, and/or possibly immunologic function.

CHAPTER I

INTRODUCTION

Forms of magnetic therapy are used everyday by millions of people. Magnetic use extends far greater than just to hang items from a refrigerator. Many people have found that by applying therapeutic magnets to their body, they get relief from the usual aches and pains they experience. There is a lot of questioning as to whether this type of treatment has a placebo effect or if actual benefits may arise from the application of therapeutic magnets. Research continues to grow throughout the world in the area of magnetic therapy to determine the efficacy of magnetic treatments, the potential benefits of a magnetic field, and the effects the human body can achieve from a generated magnetic field.

The use of magnets for therapeutic reasons began eons ago. The first usage of documented magnetic therapy was found in Chinese writings around the time of 2000 BC.[1] It was also documented that in the mid 1700s the first president of the United States, George Washington, received magnetic therapy for pain.[2] One of the oldest thesis on magnetotherapy is that of Eydam I. in 1843 which discussed the idea of surrounding the human body with a magnetic field for therapeutic purposes.[3]

It has been suggested that magnetic treatments have the potential to assist in decreasing the pain and inflammation connected with sprains, headaches, muscle soreness, inflamed joints, back injuries, and countless other related injuries.[1,3-5]

Proposals have been made claiming magnetic therapy is beneficial in the healing of wounds associated with pressure sores and diabetic ulcers. Therapeutic magnets are reportedly effective in decreasing symptoms of diagnoses such as, peripheral neuropathy, chronic pelvic pain, Parkinson's disease, osteoarthritis, chronic low back pain, fibromyalgia, and multiple sclerosis. This is just a small sampling of the vast array of diagnoses that research currently claims show beneficial affects from magnetic therapy.

For the purpose of this literature review I will specifically look into the benefits that electromagnetic therapy can bring to people with multiple sclerosis. Static magnetic fields differ from electromagnetic fields in that with the latter an electric field presents itself. However, electromagnetic fields in the extremely low frequency ranges have only a minor electrical component with the magnetic field being the primary actor.[2] The science behind the two are similar as are the mechanisms by which both static and electromagnetic fields interact with biological systems. Discussion of electromagnetic fields will be more detailed in Chapter III.

The contents of this review will start with a simplistic explanation about the science behind magnetic fields and the effects caused by their fields of force. There will also be a discussion of how the human body is affected by the electromagnetic field, including a look at the affect at the cellular level and on the central nervous system with emphasis on the pineal gland. Lastly, I will look into the effects of an electromagnetic field on multiple sclerosis, specifically through multiple case reports of experiments that have been performed.

CHAPTER II

COMPONENTS OF A MAGNETIC FIELD

The actual magnet that is used for therapeutic purposes is quite different from that of a common refrigerator magnet. The strength of most refrigerator magnets have an intensity of 10 gauss.[1] In comparison, in order for a therapeutic magnet to have an effect on the human body, the strength must be 500 gauss or greater.[1,3] Gauss is a unit of measure that measures the flux intensity of the magnetic field emitted from the magnet.[1,3,4,6] Tesla (T) is another term that reports the flux intensity of a magnetic field, it varies from gauss only in the size of the unit, 1 T is equivalent to 10,000 gauss.[4,5] The gauss of a magnet can be derived through an extensive formula (the Gauss Law) and technological, scientific equipment.[6] This law will not be discussed further in content of this review.

A magnet's frequency is measured in hertz (Hz) and the frequency varies from magnet to magnet. The higher frequencies are used for diagnostic purposes, such as x-rays, and are considered harmful to the human body under the conditions of excessive exposure.[5] The low range frequencies are the electromagnetic fields that have been found to have beneficial effects for the human body[5], low-level frequencies are considered to be those magnets with 0-300 Hz frequencies.[2,7-9] These electromagnetic fields have been found to be most beneficial when utilized in a pulsating field.[5] Within this frequency range it has been discovered that insignificant thermal effects result, in fact thermal

effects are only produced from the weak currents that are created on the extracellular side of the cell.[2]

With the application of an external, pulsating magnetic field to an electrically conductive material (i.e. any living matter, such as the human body) an electric field is induced in a perpendicular direction to the magnetic field vector in accordance with Faraday's Law concerning induction.[2,9] According to Faraday's Law the stimulating current is proportional to the rate of change the magnetic field has.[10] The magnetic field is also proportional to the current producing magnetic coils that comprise the magnet. Therefore the stimulating current from the magnet is proportional to the duration of each pulse in a pulsating magnetic field. It is by the definition of Faraday's Law that we are able to derive that an externally placed magnetic field will create an electromagnetic atmosphere within the living tissue.[9,10]

Not only do magnets have varying intensities and frequencies, but also there is an inherent presence of poles in all magnets. As we know magnets contain north and south poles; these poles constitute the magnets ability to affect the human body as long as the gauss is adequate.[5] It has been suggested that these poles create part of the over all effect on the human body via the attraction or repulsion of charged particles within the magnetic field. The charged particles are the ions that compose the human body allowing a reaction to occur.[5]

The Lorentz Force Law also comes into play when discussing magnets.[2,6,11] The Lorentz Force Law is applicable to magnetotherapy because the law applies to charged particles moving within a magnetic field. The force on the charged particle is radial and proportional to its charge, the velocity it travels, and the strength of the magnetic field.

The Lorentz Force Law determines the pathway the ions will take within the magnetic field.[6,11] In theory, with the application of a magnetic field to the human body, the ions are acted upon by the magnetic field creating effects on the nervous system, metabolism, oxygen availability to cells, blood flow, hormone release, as well as the functioning of various systems throughout the human body.[1,4]

It has been scientifically reasoned that low frequency electromagnetic fields have only a minimal ionizing effect, if any effect at all, when applied to the human body.[2,10,11] Therefore the effects of the electromagnetic field would not be explainable by an ionizing condition. In this situation, it has been hypothesized that the effects received from an electromagnetic field on the human body may be caused by physiological means of modifying hormones and growth factor interactions with receptors on the surface of body cells.[7,8,12-15]

The component parts of the magnet that allow the magnet to produce an affect on the human body are very detailed and require an in-depth look into the field of physics, for the scope of this paper the component parts of the magnet need only be simplistic. The previous is a simplistic look at a very complicated topic. Magnets are easily understood alone, however with application to the human body they become complex and some aspects are yet to be determined and at this time remain hypothetical.

Not only can electromagnetic fields be applied to the human body, but the body generates its own electromagnetic field.[12] A magnetic field also exists throughout the earth, as is well known by the presence of the north and south poles of the earth.[1,3,4] There have been various hypotheses that take the body's own generated field as well as that of the earth's into account. Dr. K. Nakagawa has proposed the idea that over the

millions of years the earth has been in existence, the strength of the magnetic field has progressively been decreasing.[3] With this concept in mind, he has come to a scientific hypothesis that the interaction of the body's generated magnetic field along with the earth's less powerful magnetic field has left the human body with a deficient magnetic field and that is the reason behind why the application of magnetotherapy is beneficial.[3] This idea is only presented to illustrate a single theory that accredits the decreasing strength of the earth's magnetic field as the reasoning behind why magnetotherapy is beneficial. This theory is that of non-Western medical professionals and will not be further discussed in the remainder of this paper.

To date, the exact mechanics of the electromagnetic field on the human body is still very unclear. Scientists are aware of the fact that electromagnetic fields have an effect and they continue to search for the answers to this and many other questions. It has been proven that if electromagnetic therapy is more than a placebo effect, it is most definitely not a cure but may have the potential to reduce various symptoms that accompany injuries and diagnoses.[12]

CHAPTER III

EFFECTS AT THE CELLULAR LEVEL

In the previous chapter, the concept of the modification of receptor sites in a low frequency electromagnetic field was briefly introduced as a key element of the ability of a magnetic field to have an effect on the human body. With this in mind we will turn the discussion towards an in depth look at the supporting science behind this concept.

A promising hypothesis is the ability of low frequency electromagnetic fields to affect specific tissues.[2,7] Conceptually, this can be analogized to the ability of a drug to work by targeting specific tissues within the biological system.[7] One proposed target tissue is the cell membrane. With this as the main key element, various changes would be produced throughout the body.[2,7,9,13,14,16]

Eucaryotic cells are multi-membraned and have a high degree of molecular structure.[2] The cell membrane is composed of counterions, glycoproteins, ligand receptors, and two layers of phospholipids. It is these molecules that determine the specificity of function of each individual cell and regulate all trafficking in and out of the cell.[2,17] The presence of an electromagnetic field may cause these membrane components to re-orientate to each other and cooperatively affect the functioning and permeability of the cell membrane.[2,16,17] With these alterations would come modifications in the sensing system of the cell that detects changes in the external environment. This would explain a minute part of the overall affects that an electromagnetic field appears to have on a body.

The overall role of the cell membrane, in living cells, under the conditions of a low frequency electromagnetic field appears to have great significance other than just the re-orientation of it. With the cell membrane being the target tissue of low frequency electromagnetic fields the transport processes and signaling system between living cells would be modified,[7-9,13,14] as well as membrane permeability.[2] An alteration in the signaling system would result in altered communication between cells that is essential for the cells to act as a whole.

Before we further discuss the cell membrane as the primary target tissue of the electromagnetic field, we first must discuss the signaling system and its components. The signaling system is composed of chemical messages that are transported between cells. These chemical messages consist of hormones and neurotransmitters and initiate action at the binding site of the cell.[2,14,18] The receiving end of the message, better known as the receptor, accepts these hormones. Metabolic responses are then created within the tissues. This signaling system works as a feedback loop, the response to one type of hormone will often also create a different hormone secretion that will communicate with the transmitter of the message (i.e. the endocrine gland). This two-way communication pattern allows for the controlling and maintenance of the equilibrium throughout the body and all of its living cells.

Signaling hormones bind to receptors, comprised of proteins, are on the external side of the cell membrane.[2,14,15] It is these receptors that are able to convert the extracellular message into a message that can be utilized by the intracellular components of a cell. Ligands are any agent that binds to the receptor; natural hormones are included in this category as well as any other binding agent, such as drugs. A complex is

comprised of two receptors bound together by a ligand.[15] The formation and modification of a complex through hormonal changes can lead to fluxes of ions such as calcium (Ca^{2+}).[14,15,18]

With the presence of a low frequency electromagnetic field, the ligand-receptor interactions and complexes may be modified.[2,7,8,13-15] This is virtually a modification of the binding of the chemical messages (i.e. hormones, growth factor, and/or neurotransmitters) to certain receptors.[7,8,13-15] This in turn alters the internal metabolic response of the cell and the cell surface activities. The alteration of the ligand-receptor interaction is an element of the changes within the cell membrane.[2,7,8,13,14] This is a key factor in the modification of the transport system.

Luben, Tenforde, and Kaune[7] are among the scientists, that have found scientific proof that a low frequency electromagnetic field does not have enough energy to directly modify the existing signal transport processes of the cell.[7,14] However, it is thought that the internal creation of an electromagnetic field by means of external application to the body, has the ability to establish current flows in the ionic aqueous medium surrounding living cells.[2,7] These currents around the cells are what are believed to contribute to the electrochemical changes in the orientation and alterations in the proteins and compositional structure of the cell membrane.[2,7,19] Because of the alterations in the functional orientation of the cell membrane, the intracellular components receive modified signals that create alterations in the usual biochemical and physiological responses of the cell.[2,7,14,19] Now then, under the influence of an electromagnetic field, a signal from a specific hormone would result in a different metabolic reaction than it would under normal conditions because of the changes in the cell membrane. The exact

mechanism through which the cell membrane is modified remains unknown, however there are many proposed hypotheses.

There are two general classes in which hypothetical mechanisms of the trans-membrane signaling processes can be grouped: 1) long-range cooperative phenomena in cell membranes and 2) localized interactions of external electromagnetic field with cell membrane structures.[2,7] These hypothesized mechanisms are represented in an illustration (Figure 1).

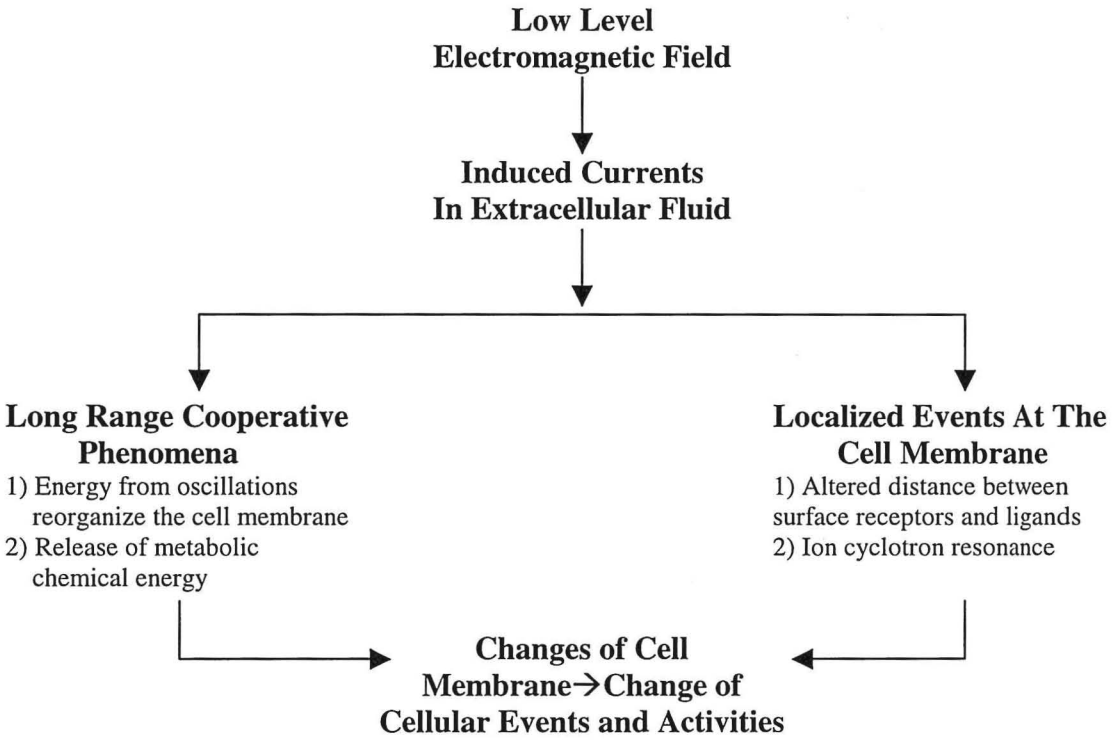

Figure 1-Hypothesized mechanisms of the alteration of the transmembrane signaling process.

Looking at the first of the long-range cooperative mechanisms requires us to take a look at an external electromagnetic field and its ability to produce cell membrane effects by comprehensive means.[2,7,16] Amplification of the weak electromagnetic field in

the extracellular fluid would be necessary to initiate long-range cooperative events within the cell. This theory exists under the hypothetical terms of 1) transition phases: oscillations that create the necessary energy to allow movement among the different energy levels; 2) charge pumping: the storage of energy from oscillations for periods of time; 3) limit-cycle models: the changing and maintenance of the cells structure through chemical reactions and diffusion; and 4) tunneling models: the ability of ions, such as Ca^{2+} to tunnel into the cell membrane changing the charge of the membrane.[2,16] It is doubtful that low frequency electromagnetic fields can successfully influence tissues solely, but with the amplification of the electromagnetic field, oscillations would be produced. The cell membrane may store the energy from these oscillations and upon reaching a greater level of energy, would release all the stored energy by reorganizing the molecules of the cell membrane.[2,7,16] It has also been suggested that the stored energy is transformed into a metabolic chemical energy that is released through ion pumps (i.e. Ca^{2+}) or enzymatic reactions of the cell membrane.[7] The basic necessity of this theory requires that the cell membrane be existent in a non-equilibrium environment that lacks stability in order to be significantly affected by weak electromagnetic fields with a collective end product of changed molecular composition, therefore creating alterations in cell membrane permeability.

Moving onto the second mechanism leads to a more appealing concept. That is the low frequency electromagnetic field interacting with living cells at a specific location on the cell membrane.[7] Experimental evidence suggests that the specific location may possibly be that of the ligand-receptor interaction at the cell membrane level, as already discussed, or possibly the movement of electrolytes across the cell membrane.

The first explanation has been developed by Chiabrera and his associates.[7] Their model explains how the low frequency electromagnetic field may modify ligand-receptor interactions. This is achieved through increasing the average distance between the receptors on the cell surface and ligands.[7,15] With the altered distance between the signaling components the life of the ligand-receptor complexes is shortened, and the ligands potential of productivity is minimized.[15] It is anticipated that this effect influences a number of biological processes, including the gating mechanism of ions in and out of the cell.[7]

The second proposal is the role of ion cyclotron resonance effects in the low-level electromagnetic field.[2,7] Research has led scientists to believe that the presence of an electromagnetic field may affect the dielectric properties via the Lorentz force component.[2,7,20] In its most simplistic form this concept implies that the electromagnetic field has the ability to displace and/or deform polarized molecules that comprise the ion channel and transfer kinetic energy to surrounding ions. This would modify the entire ionic flow.[2,7,21,22] This theory becomes very controversial as many scientists argue that this is improbable to obtain enough energy to allow the transfer to the molecules of an ion channel under a low frequency electromagnetic field.[2,7,21,23,24] In hopes of clarifying the use of the phrase ion cyclotron resonance, Lednev[21] explains that only under the conditions of an excessively high intensity can an electromagnetic field cause ions to attain the essential cyclic motion of true cyclotron resonance. However, Lednev further writes that experimental research has determined that the ion channels of the cell membrane can create the essential conditions for the existence of ion cycling under a low frequency electromagnetic field.[2,21] Feasibility of such would be under the condition of

transference of energy from the electromagnetic field to the involved ions. This would sequentially alter the ions metabolic activity and possibly the interactions of ions with surrounding ligands. With all of the conflicting impressions scientists have obtained, research will continue along the lines of this theory, as it is still immature in its form.

Although the exact mechanism of how electromagnetic fields interact with functioning of cells remains hypothetical in explanation, calcium has been studied in a variety of settings, in search of a clear understanding of the role it and other ions may play when impacted by an electromagnetic field. This role may be secondary to interactions of the electromagnetic field and ion channels or direct interaction with the electromagnetic field and the ions.[2,9,12,17,20] Calcium has been the chosen ion of study because it plays such a large role in so many molecular activities throughout the body. Calcium metabolism appears to undergo many variations in concentration, flux rates, signaling transduction, and amplification under the influence of an electromagnetic field.[2,9,20] It has been suggested that the electromagnetic field must convert its form of energy into a chemical change that would produce an inclusive effect, this may be achieved through Ca^{2+} binding to other proteins, such as calmodulin or protein kinase C, to modify and activate different signaling pathways. The activation of Ca^{2+}, by some means, can directly affect select enzymes which can alter hormonal signals, fluxes of ions, production of neurotransmitters, intracellular activities and overall cell metabolism.[2,14,20,22] The role of Ca^{2+} is also active in the binding of messages to receptors.[2,9] Calcium is present when a ligand is bound to a receptor, thus when the concentrations of Ca^{2+} are altered the entire cell's activities are affected because of the disturbance in the signaling system.[9]

Adey-Davydov[2] proposed that the electromagnetic field interacts with the phospholipid layer of the cell membrane. Normally the phospholipid layer is composed of a complex of phospholipids and calcium, denoted COO^--Ca^{2+}, but with the presence of the electromagnetic field the bonds between the COO^--Ca^{2+} complexes weaken and the Ca^{2+} is released into the extracellular space, this would create an efflux of Ca^{2+}. What is left of the bond would then be free to bind to glycoproteins on the outside of the cell membrane. The energy involved in the binding would then be transferred to the intracellular area altering the chemical and enzymatic activities in the cell.

It has also been suggested that the electric component of the electromagnetic field is responsible for Ca^{2+} behavior more so than the magnetic component.[2] If such is true then it is not feasible to explain Ca^{2+} behavior under the extremely low frequencies with which documentation is concerned. Control of Ca^{2+} with the presence of an electromagnetic field may go back to changes in the cell membrane and reorientation of ion channels as has already been discussed. Until more information is obtained, research will continue in the areas of Ca^{2+} interactions with neurons, at synapses, within the signaling system, as well as all the other molecular activities that Ca^{2+} helps mediate.[2]

The cell membrane has many unique properties that lead scientists to theorize that it plays a very important and large role in electromagnetic therapy. The membrane structure, communication system within and between various cell membranes, and the involved ions and channels through which they travel may all contribute to the solution of what remains the perplexing phenomenon about how and why the magnetic component of the electromagnetic field affects biological systems. The exact mechanism of how the electromagnetic field can affect Ca^{2+} remains unclear. Likewise, the electromagnetic

field may act directly on ions such as Ca^{2+} or the ions may be involved due to a secondary affect of the cell membrane influenced by electromagnetic field, research continues along these lines in search of the specifics.

CHAPTER IV

ELECTROMAGNETIC FIELDS AND PINEAL FUNCTION

The pineal gland is located inferior to the splenium of the corpus callosum and superior to the colliculi of the midbrain, this is illustrated in Figure 2.[25] It enables the information obtained by the visual system, from the environment, to be transformed into hormonal signals of melatonin. These signals are sent out to other organs and systems throughout the body via the blood stream.[26-28]

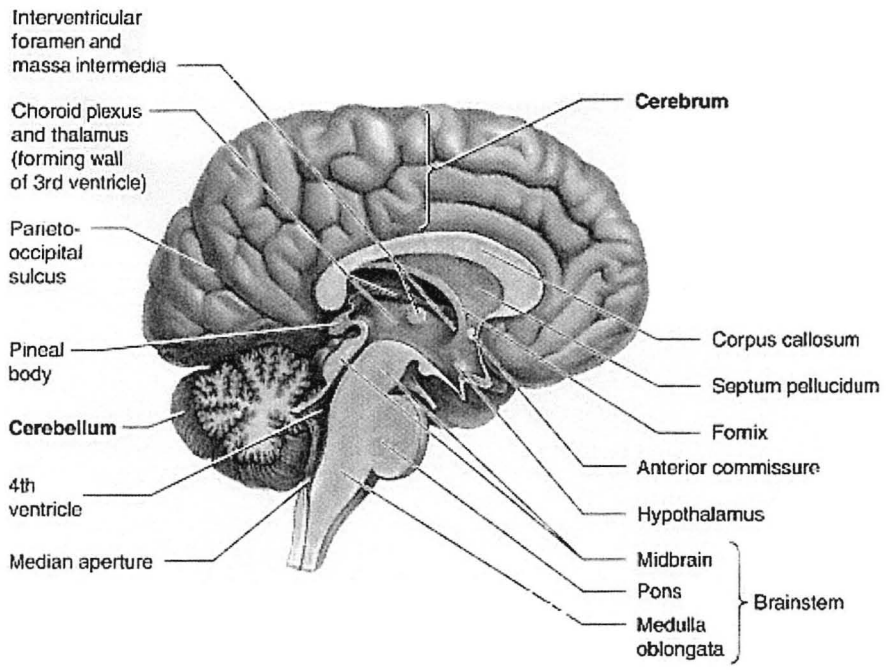

Figure 2: Illustration depicting the location of the pineal gland in reference to surrounding structures. Reprinted with permission from Moore KL & Dalley AF. Clinically Orientated Anatomy. 4th ed. Baltimore, Md: Lippincott, Williams & Wilkins; 1999:888.[25]

The pineal gland possesses the ability to affect the emotional state; the function of the reproductive system; endocrine functions such as the thyroid, pituitary, and adrenal glands; non-endocrine functions such as sleep cycle, and motor activity; and most importantly receptors for various hormones, enzymes, and neurotransmitters.[2,26,29,30] Its relevance to treating people with diagnoses such as multiple sclerosis (MS) will be discussed in the following chapter, but first we will discuss the pineal gland and the components that account for the cause and effect relationship to the electromagnetic field.

Overall the pineal gland has been termed the "Zeitgeber" which is defined as a synchronizing agent.[2,26,29] In terms of the human body, it can be explained as the gland which synchronizes all of the systems and hormonal requirements of the body. The pineal gland acts as an intermediary between the endocrine, nervous, and immune systems which allows for continuous communication and control among the three components.[2,26,29,30,31] This is accomplished by influencing hormone uptake and secretion, protein synthesis, enzymatic function, and neurotransmitter levels by secreting melatonin.[29]

Melatonin is the chief hormone of the pineal gland. However, numerous other hormones and neurotransmitters are affected by the pineal gland and the melatonin it secretes. Melatonin is synthesized in the pineal gland and is a derivative of complex enzymatic interactions with serotonin.[8,26,27,29,31] Melatonin has been found to influence neural excitability in the brain stem, alter axonal transport in peripheral nerves, and modify humoral and cellular immune responses.[32-34] A dysfunctional pineal gland may also enhance the T-cell mediated autoimmune reaction.[30,33,35] Because of these

comprehensive abilities we turn to the pineal gland, and all the hormones under the influence of the gland, in search of an explanation for beneficial effects.

The circadian rhythm controls the biological synthesis and release of hormones and neurotransmitter substances.[26,27,31] This 24 hour cyclic period is essential for the well-being of the human body and is a major influence to melatonin secretion.[8, 26,27,29,31,34] It develops a cycle of highs and lows that is dependant on visual stimulation from the lighting conditions in the surrounding environment. With increased presence of light, melatonin secretion is decreased. Likewise, in the presence of decreased available light melatonin levels increase in the blood stream, reaching their peak availability during the darkest hours of the day. The presence of an electromagnetic field alters the circadian rhythm, hence the production and secretion of melatonin is influenced, this in turn modifies the action of numerous other biological activities.

Studies have suggested that particular cells of the pineal gland are sensitive to the presence of a magnetic field around the body of birds, mammals, and humans.[21,30,36-38] This has been determined in part by the consistency that the pineal gland shows with exposure to external low frequency electromagnetic fields across and within subjects from the respective species.[27] Contrary to initial studies, it is more probable that the pineal gland is indirectly affected by low frequency electromagnetic fields.[26,31] The actual cause of changes in pineal functioning appear to be the result of altered neuronal signaling to the gland.[26,31,39] These neuronal changes would occur secondary to the changes in the Ca^{2+} transport mechanism, which were discussed earlier.[31]

In light of current research, it is believed the retinas are magneto-sensitive and play a role in signaling changes.[2,26,27,28,30,32,39] When the electromagnetic field is

intercepted by the retinas, the transport signals from the retinas to the pineal gland are modified and altered neuronal messages are sent to the pineal gland. This in turn creates changes in the functioning of the pineal gland. This theory is supported by the fact that the activity of the enzymes that synthesize melatonin are regulated by nerve fibers originating from the retinal regions.[31] Therefore, the visual system is an integral part of the production of melatonin, not only for synthesis, but also for the development of the circadian rhythm as was discussed earlier.[26,27] Either through the pineal gland solely, coupling with the retinas, or a combination of both, the pineal gland responds to the intensity of an external electromagnetic field by alterations in hormone activity, whether it be secretion or uptake, which virtually affects all biological processes.

The reaction of melatonin to a low frequency electromagnetic field has received attention from many, and numerous experiments have been performed in order to research the effects of the field on the pineal gland and the circadian rhythm. Experimentation involving an electromagnetic field's influence on melatonin, have revealed that exposure to a low frequency electromagnetic field inhibits the synthesis and secretion of melatonin.[2,26,27,28,30,32,39] Lerch, et. al.[26] and Semm[32] found, through separate experiments, that exposure to an external electromagnetic field caused a reduction in melatonin concentration.[26,28,32] Semm[32] made the following discovery: after thirty minutes of exposure to the electromagnetic field the melatonin concentration had decreased by seventy percent. An experiment similar to that of Semm's was performed in a Stockholm laboratory. This experimentation revealed conflicting results with no significant difference between the control group and the group exposed to the electromagnetic field.[28] Further testing has been performed discovering that in fact there

is a decrease in melatonin following exposure to an external electromagnetic field but it is not a permanent condition.[27] Within approximately three days melatonin levels return to the pre-treatment cyclic production and secretion levels. This is dependent on the number of electromagnetic treatments issued and provided that the magnetic field is removed.

Studies found that decreased levels of melatonin led to increased levels of serotonin (5-HT) and a metabolite of 5-HT, which is 5-HIAA (5-hydroxyindole acetic acid).[27] Normally the cyclic release of norepinephrine, due to the circadian rhythm, activates the pineal gland to produce melatonin by activating N-acetyltransferase (NAT) and hydroxy-O-methyltranferase to interact with 5-HT.[8,27,31] These specific enzymes, NAT & hydroxy-O-methyltransferase, are necessary to change 5-HT into melatonin and are inactive during electromagnetic exposure.[8,27,31,39] This inactivity allows for 5-HT and 5-HIAA to collect due to the fact that 5-HT is not required for the synthesis of melatonin.[8,27,31] Melatonin is a major player in the amount of dopamine within the biological system as well, however; dopamine is not necessary for the synthesis of melatonin.[29,32,37,40] The importance of the neurotransmitters, 5-HT and dopamine, particularly to those with multiple sclerosis, will be discussed in a future chapter.

The exact mechanism of how the pineal gland alters melatonin production and secretion under the influence of an external electromagnetic field remains in theoretical terms. Suggestions are that the electromagnetic field de-harmonizes the pineal gland's biological clock and instead of producing and/or secreting melatonin, as is done normally with the circadian rhythm, the cycle is modified and changed.[26,27,28,31] Altered neuronal signals created by the presence of the electromagnetic field or the changes in the Ca^{2+}

transport due to the presence of the magnetic component of the field may also play a part in the decreased production of melatonin and those enzymes necessary for its synthesis.[22,27] The latter, changes in the transport system, is more acceptable. Studies have proven that if the central nervous system was the only component involved in the interaction of the electromagnetic field with the biological system the effects would only be for the duration of the exposure to the field. However this is not true and the effects are longer lasting than is the exposure to the field. This supports the theory that the electromagnetic field affects the ionic transport system.[22,41]

Immune function is also affected by the pineal gland. Studies conducted on rats found that induced electromagnetic fields throughout the brain increased immune functioning.[30] The response of the T-cells, which function in part to fight disease, were dramatically increased in the peripheral blood stream. Specifically the numbers of CD4+ T-cells were increased and the numbers of CD8+ T-cells decreased. It is theorized that these immunomodulatory effects are secondary to changes in levels of melatonin.

This is further supported by two studies performed by Poili, Caroleo, Nistico, and et. al.[35] and Sandyk,[42] concerning the effect of melatonin on the immune system of rats.[35,42] The results revealed that melatonin enhances immune function by producing molecules that stimulate T-cell proliferation. Under normal biological functioning this would be beneficial to a person. However with exacerbations of autoimmune disorders, increased immune functioning may be detrimental, and decreased levels of melatonin would produce a greater benefit as the immune system would not be in full function. Prior to the onset of MS, the melatonin and its ability to enhance immune function is considered essential so that the body may fight off the causatory factor(s) of MS.[42] It is

when MS has begun its autoimmune process on the central nervous system that the increase immune functioning is undesirable.

Controversy is high in this area of study. This is created by the fact that an electromagnetic field has been found to increase immune function, likewise melatonin enhances immune function. With autoimmune disorders a decreased immune system would be optimal as to not increase the process of the disease. According to scientific research neither the electromagnetic field nor the pineal gland hinders the immune system. Scientists are looking for the extent and reasoning behind why an electromagnetic field may affect the immune system of an individual with an autoimmune disorder. Research on the pineal gland continues, although it is a small organ, it is very complex and controversial in its maintenance and control of a plethora of biological systems.

CHAPTER V

TREATMENT OF MULTIPLE SCLEROSIS WITH PICOTESLA RANGE MAGNETIC FIELDS

Multiple Sclerosis

Multiple sclerosis (MS) affects approximately 250,000 individuals in the United States and an additional 8,000-10,000 new cases are diagnosed each year.[36,43] It ranks third among those diseases that are most crippling between the ages of 15 to 60 years of age.[43] The categories of MS are benign, chronic progressive, remitting or relapsing, or acute (rapidly progressive).[43,44] MS is a systemic, chronic, demyelinating disease that has a usual clinical presentation of sporadic symptoms of dysfunction of the central nervous system (peripheral nerves, cerebellum, cerebrum, brainstem & spinal cord).[36,37,42,44,45] These unpredictable episodes occur over a period of time and have a multitude of varying extents. The most commonly seen clinical features are gait impairment, muscle weakness, spasticity, paresthesias, incoordination, loss of balance, tremors, visual disturbances, dysarthria, bowel and bladder dysfunction, depression, and cognitive impairment.[36,44] The two most common types of tremors associated with MS are intention tremors which occur only during movement of a body part, and static tremors which occur in still positions.[46]

Pathologically, there is an occurrence of an inflammatory response in the central nervous system (CNS). This response activates T-cell lymphocytes and macrophages,

suggesting an immunologic etiology.[36,37,42,44,47] Irregularities occur in the numbers of CD4+ and CD8+ T-cells present within the blood stream.[42,47] The normal function of these cells is to regulate the immune response, because of the alterations in their number they do not perform their job adequately. The exact cause of the MS remains unknown. Many hypotheses are in existence to the etiology of MS. One hypothesis that is given high regard is an etiology stemming from a viral origin that creates an autoimmune response aimed at myelin tissue surrounding the nerves of the CNS.[36,37,44]

Instead of the myelin or myelin protein as the target for the pathology of MS, some scientists theorize that the blood brain barrier (BBB) is the target.[33,37,40,45] The BBB that surrounds and protects the brain is of particular interest in the cause and exacerbations of MS. Increased permeability of the BBB leaves the barrier in danger of disruption to immune function.[45,48] This vulnerability is associated with inflammatory and progressive lesions of neural tissues, allowing for the irreversible progression of MS. This loss of integrity of the BBB plays a large role in the progression of MS.[45,48] The compromised BBB allows lymphocytes and monocytes of the autoimmune process to seep through the membrane causing further damage to adjoining neural tissues.[33,45,48] The extent of damage is allied with the duration of permissible leakage of inflammatory cells through the BBB.[48] Repeated alteration in the BBB leads to the exacerbation and remissions of MS. Each time the permeability is impaired, the risk of further demyelination increases depending on what structures get involved.[45] In fortunate cases clinical symptoms will not be present with demyelination.

Changes in the BBB may result from numerous things, such as the presence of a viral infection, or an increase in the temperature of the surrounding environment.[45] A

study performed by Devoino, Idove, Alperina, and et. al.[49] found that increased amounts of 5-HT (serotonin) inhibited immune system functioning, and T-suppressor cells were activated in bone marrow.[49] This leads to the belief that increased amounts of 5-HT would benefit people with MS, as it would act on the dysfunctional immune system to cease further autoimmune activity.

Another suggestion that has been made in the etiology of MS is the possibility that a dysfunction at the synapses, secondary to lack of neurotransmitter or receptor blockade, may be included in the etiology.[22,32,37,50] This too would account for symptomatic neuronal changes that occur with MS.

There has yet to be discovered a way to arrest or reverse the course of MS. Numerous pharmacological agents and physical modalities exist in attempt to slow the effects of MS, however no first-rate treatment has yet to be discovered.[36,44] The most frequent approach for treatment is to treat the symptoms of the disease. Several drugs exist that try to counter spasticity, fatigue, paresthesias, pain, incontinence, and depression. People with MS are urged to stay in environments that are cooler and have lower ambient temperatures.

Multiple experimental studies have found external application of low frequency electromagnetic fields to be effective.[32,33,36,37,40,43,46,50] Reuven Sandyk, a professor of neuroscience, has done extensive studies on this as well as with the treatment of Parkinsonism. However, only small cohorts have been used with both diagnoses.

Previously, it was stated that a therapeutic magnetic field must meet certain intensities before it can be considered therapeutic.[1,3] However, scientists have corresponded several accounts of patients that have been treated by means of

electromagnetic therapy with intensities in the picoTesla range coupled with low frequency strength. [32,33,36,37,40,43,46,50] One picoTesla (pT) is equivalent to 10^{-12} T,[51] therefore defying the previously stated required intensity of 500 gauss (.05 T), but yet still remaining within the range of beneficial low level frequency.

Experimentation has determined that subjectively most patients found their symptoms improved following electromagnetic therapy. [32,33,36,37,40,43,46,50] These symptoms include such things as dizziness, intermittent vertigo, fatigue, headaches, bowel and bladder dysfunction, paraesthesias, depression, sexual dysfunction, poor sleeping ability, cognitive function, and overall general mood. Objective improvements were also noted in the patient's: ataxic gait, balance skills, strength, motor control of upper and lower extremities, use of assistive devices for ambulation, general mobility, diplopia and blurred vision, incoordination, and dysarthria. [32,33,36,37,40,43,46] A few patients reported that following electromagnetic therapy they were less sensitive to heat[32] and others reported their symptomatic tremors also diminished following the therapeutic treatments.[46]

Sandyk's extensive studies have looked into the beneficial effects of electromagnetic therapy for patients with chronic progressive or chronic relapsing-remitting categories of MS. [32,33,36,37,40,43,46] Sandyk issued these treatments to patients in both categories of MS, during acute exacerbation and remittance. The patients he has treated have been treated with an extracranial electromagnetic field with an intensity of 7.5 picoTesla and frequency in the low level ranges of 2-7 Hz. [32,33,36,37,40,43,46] The device he employed to create the extracranial electromagnetic field is one that Sandyk has personally developed, the Sandyk Electromagnetic Stimulator. Duration of the

treatments ranged from 7 to 30 minutes. In select cases a patient would receive two successive treatments separated by a 15 minute rest period. Each patient received multiple treatment sessions, some received treatments in consecutive days while others would receive treatments two or three times a week. Sandyk's method for determining duration and frequency of treatment was not clarified; however, it can be implied that it was determined by the severity of the illness and the goal of the experimental treatment.

Other scientists carried out experimentation involving the use of the Enermed device, which creates a low frequency electromagnetic environment with an intensity of 4-13 Hz.[50] This device, is the size of a wrist watch and is worn on an acupuncture point for two months. The subjects were placed in one of four cohorts. One cohort used a placebo device on a given acupuncture point while the other three cohorts had the device placed on an acupuncture point of the shoulder, back, or hip. This experiment revealed statistically significant improvement in patient reported performance, especially in the symptoms of fatigue, bladder control, and spasticity. The Extended Disability Status Scale (EDSS) was used as an objective measure in the experiment; however, the results revealed no significant difference between pre- and post- treatment. It is pointed out that the functional tool used for measurement is a measure of gross mobility. Although objective measurement is extremely important, the fact that the patients reported subjective improvement may have an equal importance in regards to function.

To date, no adverse side affects have been reported by any subject that has endured experimental studies with electromagnetic therapy. These treatments are considered safe and harmless as has the general use of magnets for therapeutic purposes.[7,13,21,32,33,36,37,40,43,46,50] In a select number of cases utilizing the Enermed device,

there was a reported increase in occurrence of headaches. This was not observed in other groups that were wearing the magnetic devices for longer time frames nor in any of Sandyk's cohorts. There may be other external factors in the increased number of headaches people experienced, keeping in mind that occurrence in one individual would affect the overall outcome.[50] There was also a few subjects that experienced an increased amount of depression, however, these people also experienced such during time periods of wearing the device as a placebo effect. Headaches and/or depression do not appear to be correlated with the application of a low frequency electromagnetic field.

The overall mechanism by which an external low frequency electromagnetic field can produce such improvements in disorders such as MS remains unknown, however many hypotheses exist.[32,33,36,37,4.,43,46,50] These hypotheses are along the lines of the information that has been presented in the previous chapters. The following explains and clarifies how the electromagnetic field may benefit those people with multiple sclerosis in terms of the content of this paper.

Multiple Sclerosis and the Cell Membrane

If in fact application of an external electromagnetic field does alter the fabrication of calcium membrane binding and ionic cycling, it would in turn affect the excitability of the cell membrane leading to neuronal changes within the body,[33,36,37,41] including increased neural transmission and the propagation of transmembrane signals,[33,40] all of which would benefit the symptoms of MS. At the cellular level, transmembrane calcium flux would not only influence the state of the resting membrane potential but also increase the amount of neurotransmitter release.[40] This would virtually affect the happenings within the cell due to excitability changes in the neural and cellular

membranes. The conduction abilities of sensory and motor messages along the nerve fiber and at the synapses would be altered due to changes in the Ca^{2+} concentration.[33] Alterations at the cellular and neural levels are vital in the explanation of the interaction between the external electromagnetic field and a biological system.

Multiple Sclerosis and the Pineal Gland

Dysregulation of pineal function may be a factor in the pathophysiology of MS. The rationale of applying low frequency electromagnetic fields for therapeutic purposes to people with MS comes from the fact that the pineal gland has such great influence over neurotransmitters, the immune system, and a multitude of biological functions.[30,32,33,36,37] Sandyk coined the pineal gland a "pivotal mover" because this gland may act as a constituent in the activation of MS, as well as responsible for the relapsing-remitting course of the disease.[32,36,37]

In one particular experimental study, Sandyk tested the role of an external electromagnetic field and the effects it would have on the pineal gland.[36] The patient, a 50 year old woman, initially received magnetic treatments for three months, each session was seven minutes long, at a frequency between 2-7 Hz, and had a static intensity of 7.5 pT. The patient reported that her symptoms had greatly improved following the magnetic treatments. The exact number of treatments she received was not stated. The patient was then challenged with oral melatonin, a dose of 3 mg.

Roughly one hour after the oral dose of melatonin the patient experienced an exacerbation of her symptoms.[36] She reported decreased strength in her lower extremities, and increased incoordination. She was unable to ambulate with ease, falling twice in one trial, she experienced urinary incontinence, dizziness, vertigo, and blurred

vision. Objective examination revealed nystagmus with lateral and vertical gaze, diplopia with lateral and upward gaze, a positive Romberg test, and intention tremors with finger-to-nose and heel-to-knee testing. Her gait was very ataxic with a very broad base of support. Her vitals were as follows: blood pressure (BP): 170/100 mm Hg and heart rate (HR): 92 bpm, following the administration of melatonin. Prior to the dose of melatonin her vitals were: BP: 120/60 mm Hg and HR: 50 bpm. On initial assessment, her vitals were significantly higher; BP was 150/60 mm Hg and HR was 64 bpm.

Sandyk hypothesized that if in fact an external electromagnetic field could effect the release of melatonin via the pineal gland by decreasing the concentration of melatonin released, an extracranial electromagnetic field treatment would benefit the patient.[36] The scientist proceeded to treat the patient for seven minutes with a sham field, the 60 minutes following the sham treatment produced no changes in her condition, neither subjectively nor objectively. Subsequently a seven-minute extracranial electromagnetic field treatment was issued to the patient using the same intensity (7.5 pT) and frequency (2-7 Hz) as in the initial treatments, before the oral dose of melatonin was taken.

Within a half and hour after the extracranial electromagnetic treatment the patient reported she felt more energetic.[36] Again her vitals were taken to reveal a decrease in her blood pressure to 140/70 mm Hg and a heart rate of 74 bpm. Another 15 minutes passed by, the patient reported that the feelings of dizziness and vertigo had passed, her diplopia had ceased, and her strength, coordination, and balance had all improved. The patient reported 50 to 60% improvement following electromagnetic treatment, this was supported by Sandyk's objective neurological evaluation. Objective findings discovered improved gait patterns and cerebellar maintained abilities, better articulation of her

speech, ability to tandem walk, negative nystagmus tests bilaterally, and only mild intention tremors were observed in the finger-to-nose test.

A similar experiment was done with all the same variables but with a 27 year old female patient whom had MS.[36] The results were very similar to those discussed above. Forty minutes after the oral dosage of melatonin was given the patient experienced an exacerbation of symptoms; electromagnetic treatment again reversed the affects of the oral melatonin 15 minutes after the electromagnetic field ceased.

The method of melatonin inhibition by the external electromagnetic field was discussed in Chapter IV of this review. These two case studies support the hypothesis that increased levels of melatonin may cause exacerbations of MS and the electromagnetic treatments counter these exacerbations by inhibiting melatonin release.[36] Other agents that benefit patients with MS that likewise have the effect of inhibiting melatonin release are corticosteriods and exposure to bright artificial light.

Multiple Sclerosis and Conductivity: Synapses and Nerve Fibers

Customarily, it has been proposed that the signs and symptoms of MS are present because of the demyelination of nerve fibers, resulting in slowing of the conduction of sensory and motor messages. The delayed latencies of evoked potential responses, which are a hallmark of MS, are also thought to be caused by the demeylination along the nerve fibers.[37,40,52] Contrarily, demyelination may only be one possible solution to the proposed dilemma. The possibility exists that deficient neurotransmitter substance or blockade of receptors may delay latencies that are discovered with evoked potential studies.[37,40,50,53,54] This theory is supported by findings of demyelination present in cadavers who never experienced neurological deficits prior to their deaths despite the lack of myelination.[37]

The only way this trademark of slow conduction is reversed is with the remyelination of involved nerve fibers.[37,53] If we consider only the demyelinating component of MS, it is very difficult to explain how the symptoms of MS can occur so abruptly with exacerbations. The fact that patients receive such prompt, positive effects after the application of an extracranial electromagnetic field coincides with the notion that the primary cause of MS is deficit synaptic conductivity.[37,53] Such prompt benefits from electromagnetic treatment is difficult to explain in terms of remyelination since the remyelination process takes several weeks to months.[37,40,53]

Further supporting data to the hypothesis is found in Sandyk's studies. Findings report that the application of extracranial electromagnetic fields are beneficial to visual and brainstem auditory evoked potentials, VEPs and BAEPs respectively.[32] Because abnormal latencies of VEPs and BAEPs are a reliable, consistent characteristic of MS, they have been referred to for some time in the diagnosis of MS.[32,37,40,50,52,54] Evoked responses provide information on how the central and peripheral nervous system is functioning.[47] Prolonged latencies found via evoked potential studies are coupled with a decreased conduction velocity. The decreased amplitude, revealed through evoked potential studies, is associated with the extent of conduction blockage along the nerve. This is essentially determined by the severity of dyemyelination.[32,40] Specialized equipment is used to record the electrical activity that is created by the stimulation of the sensory nervous component of the CNS.[47] VEPs and BAEPs are obtained by cortical stimulation by watching reversing patterns on a screen or by listening to sounds which are intended to stimulate the brain stem. In Sandyk's studies, he used a reversing sequence of black and white checkerboard on a screen to stimulate visual responses.[32,40]

During cortical stimulation, one eye at a time is stimulated and the non-involved eye is covered with a patch. While the eye is stimulated an electroencephalogram reading is taken from the occipital region bilaterally via electrodes. The electroencephalogram allows the properties of the waveform, the amplitude, and the latency to be recorded and studied.[47] All of these traits are compared to the normal state of these characteristics to determine the function of the transmitting element to the brain.

Normal VEP latencies range from 95 to 115 msec and normal amplitude is considered 6 to 12 μVolt.[32,40] Sandyk discovered that a 46 year old woman, who had been diagnosed with MS at the age of 36, had abnormally long latencies bilaterally as well as low amplitude of the waves prior to extracranial electromagnetic therapy. The latency, reported in msec, was 132 and 130 for the left and right occipital regions respectively, while the amplitude (μV) was 1.64 and 1.00 with left eye stimulation. During right eye stimulation, the latency and amplitude were as follows 124.8 msec & 1.30 μV for the left and 122.4 msec & 1.00 μV for the right occipital region, refer to Table 1.

Table 1-VEP Response of a 46 y/o Female Prior to Extracranial Magnetic Treatment.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	132 msec	1.64 μV	124.8 msec	1.30 μV
Right Occipital	130 msec	1.00 μV	122.4 msec	1.00 μV

Normal latency is within a range of 95 to 115 msec. Normal amplitude is 6-12μV.[29,39]

BAEPs measure the latency at several different points of the brain stem.[32] The waves are routinely measured at the acoustic nerve, pons, and midbrain. In Sandyk's studies, conduction abilities were measured between the caudal segment of the auditory pathway in the brainstem and between the rostral pontine and the midbrain.[32,52] The

results determined the latency at the pons was delayed just slightly as it was 4.224 msec bilaterally and normal is 4 msec.[32] At the midbrain there was an even greater delay of 6.384 msec on the left and 6.576 msec on the right, the normal latency of the midbrain is 6.2 msec, refer to Table 2. The sensory information is generated by the superior olivary complex at the pons and by the inferior colliculi of the midbrain. Referring back to the anatomical picture of the brain, presented in Figure 2, it can be inferred that the region between the pons and midbrain tectum is involved in the slowed conduction of the sensory information. This region has been proven as the common hindrance of BAEPs in people with MS.[32,52] In a study done with a group of 202 people that had definite, probable, or possible MS, the authors found that through BAEP studies the majority of the conduction abnormality was between the pons and the midbrain.[52]

Table 2-BAEP Response of a 46 y/o Female Prior to Extracranial Magnetic Treatment.

	Left Ear Stimulation LATENTCY	**Right Ear Stimulation** LATENCY
Acoustic Nerve	1.824 msec	2.544 msec
Pons	4.224 msec*	4.224 msec*
Midbrain	6.384 msec*	6.576 msec*

*denotes those latencies which were delayed
Normal latency at the pons is 4.0 msec. Normal latency at the midbrain is 6.2 msec.

Following three consecutive, daily treatments of extracranial applied electromagnetic therapy with a frequency of 5 Hz, intensity of 7.5 pT, and for period of 10 minutes, the VEP studies were repeated.[32] The VEPs of the left eye showed notable improvement bilaterally however they remained borderline for normalcy at 116.4 msec & 115.2 msec for the left and right occipital regions respectively. The right eye improved

to some extent, however remained out of the normal range at 129.6 & 126.0 msec for the left and right occipital regions respectively, refer to Table 3.

Table 3-VEP Response of a 46 y/o Female 3 Days Post Extracranial Magnetic Treatment.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	116.4 msec	*	129.6 msec	*
Right Occipital	115.2 msec	*	126.0 msec	*

Normal latency is within a range of 95 to 115 msec.
*Values not reported within case study

The evoked potential studies were recorded one week after the initiation of the magnetic treatments, with all variables remaining constant. This revealed that the latencies had improved.[32] The VEPs showed drastic improvement and were within the normal range of 95-115 msec. The stimulation of the left eye produced latencies of 99.6 msec & 108.0 msec and amplitudes of 3.35 μV & 2.75 μV, while the right eye stimulation produced 100.8 msec &108.0 msec and amplitudes of 1.750 μV & 2.750 μV to the left and right occipital regions respectively, refer to Table 4. The amplitudes remained significantly lower but it can be noted that those of the left eye increased a considerable amount.

Table 4-VEP Response of a 46 y/o Female 7 Days Post Extracranial Magnetic Treatment.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	99.6 msec	3.35 μV	100.8 msec	1.75 μV
Right Occipital	108.0 msec	2.75 μV	108.0 msec	2.75 μV

Normal latency is within a range of 95 to 115 msec.

The studies of the BAEPs also revealed values within the normal range for the specific areas.[32] The latency at the pons was recorded as 3.6 msec which is within the

allowed 4.0 msec and that of the midbrain was 5.568 msec which is likewise within the 6.0 msec, refer to Table 5.

Table 5-BAEP Response of a 46 y/o Female 7 Days Post Extracranial Magnetic Treatment.

	Left Ear Stimulation LATENTCY	Right Ear Stimulation LATENCY
Acoustic Nerve	1.824 msec	1.680 msec
Pons	3.600 msec	3.984 msec
Midbrain	5.568 msec	5.664 msec

Sandyk conducted a second study that again looked at the effects electromagnetic treatments had on visual evoked potentials of a 39 year old woman.[40] With this particular case the woman was receiving 1 to 2 treatments per week during a 32 month period. The intensity of the electromagnetic field this patient was exposed to was 7.5 pT and the frequency was 5 Hz, she endured these conditions for a time frame of two separate twenty minute periods with a 15 minute break between the two treatments.

Prior to any magnetic treatment, baseline VEPs were recorded.[40] The findings to these studies were prolonged VEPs. The right eye VEP latencies were recorded as 130 msec from the right occipital region and 132 msec from the left. The average amplitude was found to be 1.00 μV. Similar findings resulted in the study of the left eye as those recordings were 131 msec & 136 msec respectively with an average amplitude of 1.82 μV, see Table 6. The patient was then subjected to the magnetic treatments.

Table 6-VEP Response of a 39 y/o Female Prior to Extracranial Magnetic Treatment.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	136 msec	1.82 μV+	132 msec	1.00 μV+
Right Occipital	131 msec		130 msec	

Normal latency is within a range of 95 to 115 msec.
+Amplitude values: reported as an average of the two latency waveforms.

Twenty-three days later the VEP studies were repeated in the same laboratory under the same conditions.[40] Improvement was noted. The right eye latencies were 106 msec & 104 msec, right and left occipital regions and the average amplitude had increased to 3.87 μV. A similar report was confirmed with left eye stimulation. Latencies were 100 & 104 msec and the average amplitude was 3.69 μV, refer to Table 7. At this point in the treatment the frequency of the magnetic field was changed to vary between 5-7 Hz. This change would remain constant over the next 32 months of treatments, with treatment frequency being 1-2 times per week. Sandyk only stated that the regime was once or twice a week, he did not state how he determined this frequency.

Table 7-VEP Response of a 39 y/o Female 23 Days after Initiation of Extracranial Magnetic Treatments.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	104 msec	3.69 μV+	104 msec	3.87 μV+
Right Occipital	100 msec		106 msec	

Normal latency is within a range of 95 to 115 msec.
+Amplitude values: reported as an average of the two latency waveforms.

After 32 months had passed the patient reported dramatic improvements.[40] Prior to any treatment she had scored a 6 on the abbreviated Disability Status Scale (DSS-Kurtzke), following the 32 months of intervention she scored a 2 on the same scale. The DSS-Kurtzke is a functional measure that is commonly used during the evaluation of an individual that is affected by MS.[55] A score of 6 on the DSS-Kurtzke is obtained if the individual requires an assistive device for functional walking. The type of assistive device is irrelevant. A score of 2 on the DSS-Kurtzke is assigned to individuals with a minimal disability. This includes slight weakness or stiffness of the musculoskeletal system, mild disturbance of visual function, and/or mild gait disturbances.

It was at this time, 2 years and 8 months after the initiation of magnetic treatments that the VEP studies were conducted for a third and final time.[40] The evoked potential latencies showed drastic improvement and normalization. The right and left occipital regions of the right eye were 91.8 msec & 93.6 msec with the average amplitude of 4.15 μV. The left eye latencies were 97.2 msec & 97.2 msec and the average amplitude was 5.18 μV, see Table 8. These results revealed normal conduction rates with increased amplitudes, although the amplitudes increased, the left eye slightly better than the right, they are still considered out of the range of normal.

Table 8-VEP Response of a 39 y/o Female 32 Months after Initiation of Extracranial Magnetic Treatments.

	Left Eye Stimulation		Right Eye Stimulation	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
Left Occipital	97.2 msec	5.18 μV+	93.6 msec	4.15 μV+
Right Occipital	97.2 msec		91.8 msec	

Normal latency is within a range of 95 to 115 msec.
+Amplitude values: reported as an average for the two latency waveforms.

Combination of Components under the Influence of an Electromagnetic Field

As stated earlier the demyelination of nerve fibers may only be the result of a much more complex etiology.[32,37,53] It has been discovered that serum levels of cerebral spinal fluid (CSF) concentrations of 5-HT are decreased in patients with MS.[32,40,46,56,57] Studies conducted by Hyyppa et. al.[37] have found that dispensation of tryptophan, a predecessor of 5-HT, produced favorable effects in 50% of the tested patients with MS. A deficiency of the serotonergic (5-HT) neurotransmitter may create a dysfunction in the conduction at the synapses which may actually be the real culprit to the cause of the disease.[32,37,40,50,53]

Reports have also been published that 5-HT and its precursors perform a crucial part in the proper functioning of cerebellar activities.[46,57-59] Serotonin encourages motor control of skeletal muscles, reciprocally greater muscle use causes increased presence of 5-HT throughout the body.[58,59] The concentrations of 5-HT are controlled by the circadian rhythm and are also affected by the pineal gland. Sensory receptors have been found to be less receptive with increased levels of 5-HT. Contrarily, the more sensory action, the less concentrated the 5-HT. Serotonin plays a critical role in various CNS functions, including but not limited to: the coordination and regulation of motor control, sensory, autonomic, cognitive, affective, and endocrine functioning.[33,40,57-59]

Multiple studies have also revealed that neurotransmitters and those monoaminergic neurotransmitters that are related to 5-HT, are capable of altering the amplitude of visual evoked potential responses.[32,37,54] The results of these studies infer that visual evoked potentials respond and require the presence of certain neurotransmitters and rely on properly working synapses in order to relay messages efficiently.

As we have discussed, electromagnetic fields inhibit the release of melatonin and because the presence of melatonin inhibits the production of 5-HT and dopamine, which are beneficial in improving the symptoms of MS, the electromagnetic field actually provides a nurturing environment in the body for the production of neurotransmitters.[32,37,40] MS symptoms are improved by 5-HT and dopamine by improving CNS functioning through of the enhancement of immune function and synaptic conductivity by the involved neurotransmitters.[22,32,37,40,45,48]

Looking at the prolonged latency secondary to deficient neurotransmitters or receptor blockade leads us to the discussion of dopamine.[37,53,54] Dopamine has been determined to be important in the maintenance of normal VEPs. Studies have proven that blocking the uptake of dopamine can have a negative influence on latency times by increasing them, and administration of dopaminergic drugs, (i.e. L-dopa) can decrease abnormally long VEP latencies.[32,40,54,60]

A study performed by Jankovic, Ranin, Velijic, et. al.[30] determined the pineal gland can change the number of circulating T-cells in the peripheral blood stream. The T-cell count is indicative of cellular immunological functioning. The two types of T-cells are CD4+ and CD8+.[30,47] These fighting cells are believed to be intertwined in the etiology of MS. It is for this reason that it is important for the T-cells to be normalized. An electromagnetic field may or may not be able to normalize a dysfunctional pineal gland so that the number of T-cells is appropriate and an autoimmune reaction cannot occur, studies continue for the answer to this question.[30]

The pineal gland has the ability to influence the body in an enormous way. It affects the availability of neurotransmitters, especially 5-HT and dopamine, as well as influences the body's immune function. The presence of an external electromagnetic field that is operating in low frequency and extremely low intensity appears to enhance the functioning of the pineal gland as well as modify activities at the cellular level to benefit the ailments of the human body.

CHAPTER VI

CONCLUSION AND DISCUSSION

As common as modern medicine is to treat or prevent various health conditions, alternative medicine is on a rapid incline. The health profession is seeing a tremendous turn towards the usage of alternative means of treatment for various health care needs. Magnetic therapy, with or without a more prominent electric field, ranks highly among the most popular alternative methods of care. To date, no adverse side effects have been reported with the use of magnetic therapy. The empowerment of knowing the basic mechanisms of magnetic and electromagnetic fields broadens the reader's knowledge and clinical treatment basis.

This review looks specifically at the scientific reasoning of how an electromagnetic field produces benefits in people who have MS. The functioning of an electromagnetic field compared to a strict magnetic field is concerned with the same parameters, with the exception of the presence a much more evident electric field with the generated electromagnetic field. Although the parameters of the fields created for therapeutic purposes differed from those required for a strict magnetic field, the concept remains the same among the two types of fields. Studies have proven that the electric component of an externally generated field with such low frequencies has no affect on the matter within the field.

The science behind the effects of electromagnetic fields is very well supported by the numerous studies have been conducted. Within this review, the focus was on the

effects at the cellular level, which involved changing the cell membrane organization, and altering the transport and signaling pathways. Another primary focus was the effect the electromagnetic field posed on the pineal gland of the CNS. Interaction between the electromagnetic field and the pineal gland produced hormonal changes, immunologic modifications, and alterations of neurotransmitter presence within the biological system, this in turn affects the symptoms of MS.

Of the two main areas of concentration, the latter is more reasonable than the cellular level for people with MS. MS is caused by neurological and immunological deficits, studies have proven that an electromagnetic field has the potential to interact with the CNS and immune function through the pineal gland. Not to down play the importance of the effects at the cellular level, but with the cumulative research presented before us and knowing the physiological happenings that occur with MS, the involvement of the CNS, endocrine, and imunologic systems with the electromagnetic field appears to play a larger role than changes at the cellular level. However, it must be recognized that the cellular changes posses the ability to benefit the symptomology of MS by alterations of signal propagation, neuronal communication, and cell excitability.

Looking into the controversy of the immune system function and the ability of both melatonin and an electromagnetic field leads us to look at the scientific support. Research has determined that although the above is true, it is also true that in the pathology of MS the numbers of CD4+ and CD8+ cells are skewed. Further research may conclude that the benefits of an external electromagnetic field outweigh the negative effects of enhanced immune function. One such benefit is that by decreasing the melatonin, serotonin is increased and therefore the number of suppressor T-cells are

increased as well. Further research needs to be done in this area to determine if an electromagnetic field can affect the number of present T-cells, if so this may be added to the reasoning of receiving benefits from electromagnetic treatments. If such is not true, further information will still have been obtained regarding this area.

This review is quite thorough in researching the science behind a generated field. It is important to realize however that the research of the effects of an electromagnetic field on an individual with multiple sclerosis is highly limited to a minute number of scientists. These minute numbers of scientists have performed various studies echoing one another's results. They agree that MS symptoms may be improved with electromagnetic therapy. Another factor to point out is the lack of addressing multiple variables that were present in each of the studies. Examples of such were the headaches and depression in the Enermed studies. In Sandyk's studies, there was also the lack of stating the determinants of treatment parameters, such as number of treatments, intensity, and/or timing between treatments. These may have created different results had things been set up differently. It would be interesting to conduct further studies on these topics.

Although great and abundant scientific support is present, the actual mechanisms of action with the biological system remain hypothetical. Studies will continue in this area to put these hypotheses into more concrete theories. Many controversies exist in the physiological versus psychological means of improvement with magnetic therapy. This paper provides evidence that electromagnetic therapy appears to be a treatment option for the symptoms of MS. However, this is not to say that magnetic therapy is beneficial for all diagnoses. In order for the person to benefit from magnetic therapy the condition must be affected by alterations in the functioning of the cell, cell membrane, transport

and signaling system, ionic changes, hormonal changes, alterations in neurotransmitter substance, and/or possible immunologic function.

Being physical therapists and in such intimate contact with our patients, we need to keep abreast of current and new techniques that are available for people. If not to utilize directly in our own practice, at least, so that we may be able to direct people in the right direction in their health care and prevent them from causing themselves undue harm, turmoil, and/or cost.

APPENDIX

SCHOOL OF MEDICINE & HEALTH SCIENCES
DEPARTMENT OF PHYSICAL THERAPY
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