

Scientific Rationale for the Use of MCS on Eyes

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Introduction

Age-related Macular Degeneration (ARMD) and cataracts are the major causes of visual impairment and blindness in the United States in persons over 55 years of age. ARMD damages the retinal tissue in the macular area causing fine pigmentary stippling, retinal pigment epithelium (RPE) changes, and the development of drusen. Drusen are the precipitation of cellular waste materials in the RPE. Drusen usually occur in a mirror pattern in both eyes, but not necessarily. As you will read below, drusen typically consists of a buildup of proteinaceous waste materials.

ARMD can be wet (exudative) or dry (non-exudative). The dry type is characterized initially by either normal acuity or only a moderate acuity loss that commonly progresses to a severe central vision acuity loss. The wet type may progress to rapid and severe vision loss. At the present time there is no recognized therapy for the dry type of ARMD and the common treatment for the wet type, which must be done within 24 hours of a bleed, is laser coagulation and obliteration of the offending vessels. The percentage of md patients who benefit from this laser therapy is estimated at about 4%.¹

With dry ARMD, yellow-white deposits called drusen accumulate in the retinal pigment epithelium (RPE) tissue beneath the macula. Drusen deposits are composed of waste products from photoreceptor cells. These waste products are sometimes called discs. For reasons few people understand, RPE tissue can lose its ability to process waste. As a result, drusen deposits accumulate in the RPE. Drusen deposits are typically present in patients with dry ARMD.

The drusen deposits are thought to interfere with the function of photoreceptors in the macula, causing progressive degeneration of these cells. I do not believe that drusen are actually the primary cause of loss of VA, I believe that they are an effect of loss of energetic vitality.

As we age, the process of cell respiration produces a type of waste product called free radicals. Free radicals are "highly combustible" and promote the cells literally burning out or aging. They dramatically compromise cellular energetic

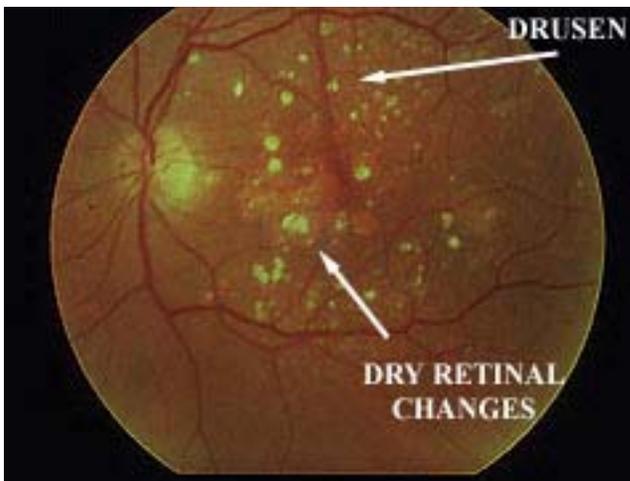
¹ Personal communication with Drs. Cousins and Margolis at Bascom-Palmer Eye Institute in Miami, 1998.

efficiency by literally burning up the mitochondria, which are the cells' energy factories. I believe that the deficient cellular housekeeping efficiency, which is directly proportional to a decrease in the intracellular concentration of ATP, is responsible for the buildup of drusen. Although drusen may block light transfer and obstruct the cell's functions, including the regeneration of rhodopsin, I believe that the drusen is a symptom of a more elemental dysfunction.

The point of minimum effort for re-establishment or enhancement of vision may lie outside the drusen mechanism. It might be theoretically possible for the drusen to stay and for the vision to be re-established, enhanced, or at least maintained. If there is actually another metabolic/biological component that is the pin upon which hinges the vision function, then we must identify and address that component.

Sources state that the drusen is a complex of up to 11 different hyaline (protein) molecules and these sources do not address a calcium component.² CMSD studies indicate that drusen are similar in molecular composition to plaques and deposits in other age-related diseases such as Alzheimer's disease and atherosclerosis.

While there is a tendency for drusen to be blamed for the progressive loss of vision, drusen deposits can, however, be present in the retina without vision loss. It is very important to keep this in mind. Some patients with large deposits of drusen have normal visual acuity. If normal retinal reception and image



transmission is sometimes possible in a retina when high concentrations of drusen are present, then even if drusen can be implicated in the loss of visual function, there MUST be at least one other factor which accounts for the loss of vision.

Retinitis Pigmentosa (RP) is a genetically linked dysfunction of the retina and is related to mutation of the ATP Synthase Gene 6^{3,4,5}

² Center for the Study of Macular Degeneration (CSMD)), University of California, Santa Barbara.

³ Molecular Biology of the Cell by Bruce Alberts, et al. - 3rd ed., Garland Publishing, Inc., New York & London, 1995.

⁴ An Introduction to Genetic Analysis by Anthony J.F. Griffiths, et al. - 5th ed., W.H. Freeman and Company, New York, 1993

⁵ <http://128.252.223.112/posts/archives/mar98/890683118.Cb.r.html>

When observing the data, which suggests that, the three of the major degenerative retinal diseases all have genetic links, a very interesting, commonality is present in all the sources. The genes which have been implicated in RP, ARMD, and Stargardt's Disease, are ALL genes of ATP metabolism. One affects the protein ATP synthase and the other affects ATP binding cassette transporter.

Several things now come to mind here which form the foundation of my hypotheses.

- 1.) ATP dysfunction seems to be the common link between the different genetically related forms of retinal degeneration.
- 2.) Enhancement of intracellular ATP concentrations is a known effect of microcurrent⁶.
- 3.) Anecdotal evidence suggests that microcurrent improves visual acuity for some macular degeneration and RP patients, and slows or stops the degeneration for others.

The logical assumption, leading to hypothesis, is that since microcurrent enhances the intracellular concentration of ATP and defects in ATP synthesis have been implicated in retinal degeneration, the application of microcurrent may provide one of the important keys to the management of ARMD.

Hypotheses

Hypothesis 1: Underlying the symptoms normally seen in patients diagnosed with ARMD is a more fundamental and elemental metabolic imbalance. A normal part of aging is the loss of efficiency of the cellular energy management systems. This is due, at least in part, to a decrease in mitochondrial function. The decrease in mitochondrial function results from free radical damage and mutation of mtDNA (mitochondrial DNA). Insufficient mitochondrial output of ATP naturally leads to low concentrations of intracellular ATP.

Hypothesis 2: ARMD is considered to be a retinal disease. I propose that this disease is much more complex than simply being a disease of the retina. I believe it is part of the age related, energy processing degenerative syndrome created by the decrease in ATP production. I also propose that one of those very complexities of vision, its dependence on ATP availability, provide the key which simplifies and unlocks the treatment of the disease.

⁶ Cheng, Ngok, Et Al., November-December 1982. "The Effects of Electric Currents on ATP Generation, Protein Synthesis, and Membrane Transport in Rat Skin." , "Clinical Orthopedics and Related Research, 171, November-December 1982, pp.264-271

Hypothesis 3: MCS has been shown to increase intracellular concentrations of ATP.⁷ The complete mechanism by which this occurs is unknown. If the aging process is truly characterized by ATP deficiencies and ARMD is truly a disease of aging, then the stimulation of ATP production could be the reason that microcurrent can aid in the control of the degeneration associated with ARMD.

Protein synthesis is enhanced by microcurrent stimulation. So is the cell's ability to absorb nutrients and to produce ATP. Currents in the neighborhood of 500 microAmps have been shown to increase ATP concentrations up to 500%.⁸ Electrical resistance of the Schwann cell sheaths is decreased by establishing an increased electrical charge on the cells and a significant amount of information is processed and transmitted, not via the traditional waves of depolarization of the cell membrane, but also via an analog current carried by the myelin sheaths.⁹

What is an increase in visual acuity? Vision is the process of transmitting information from light to the brain where it is interpreted as images. Enhancing vision is increasing the eye's ability to deliver enough signal or an adequate series of signals to the brain, to produce an image which is perceived at a level of higher resolution.

And how do you get more products (signal) to market (perception)? ANSWER: Increase the amount of information being transmitted and increase the bandwidth (eliminate the transmission bottlenecks).

Hypotheses which need to be tested eventually:

- 1.) Stimulating the eyes with microcurrent will slow, stop, and in some cases, to some degree, reverse the symptoms of Age Related Macular Degeneration.
- 2.) Stimulating the eyes with microcurrent in the presence of nutritional supplementation, specifically a combination of nutrients designed to decrease the oxidative destruction of the mitochondria and ATP synthase, will slow, stop, and/or in some cases, to some degree, reverse the symptoms of Age Related Macular Degeneration.
- 3.) A group of patients who receive a placebo or sham will show less improvement than the group receiving the real stimulation.

⁷ Cheng, Ngok, Et Al., November-December 1982. "The Effects of Electric Currents on ATP Generation, Protein Synthesis, and Membrane Transport in Rat Skin." , "Clinical Orthopedics and Related Research, 171, November-December 1982, pp.264-271

⁸ Cheng, Ngok, Et Al., November-December 1982. "The Effects of Electric Currents on ATP Generation, Protein Synthesis, and Membrane Transport in Rat Skin." , "Clinical Orthopedics and Related Research, 171, November-December 1982, pp.264-271

⁹ R. O. Becker, "The Significance of Bioelectric Potentials," Bioelectrochem. Bioenerg., 1, 187(1974).

MITOCHONDRIA AND AGING

Of the many different theories of aging, they all have the second law of thermodynamics in common. "The universe constantly changes so as to become more disordered".

THE ATP SYNTHESIZING ENZYMES OF THE MITOCHONDRIA

ATP synthesizing enzymes have been shown to suffer oxidative damage that affects the efficiency of ATP production (Shigenaga, '94, p.10775). Research has shown "age related changes of the mitochondrial energy metabolism in rat liver and heart, indicating a decrease of the ATP synthase activity, and accompanied by a decrease of the amount of beta subunit" of the F₀F₁ ATPase.¹⁰ (Kroll, '96, p.57).

Guerrieri et. al, claim to have shown functional and structural differences of the mitochondrial F₀F₁ ATP synthase complex in the hearts of aged rats (24 months old) when compared to young rats (3 months old). They relate this to the alteration of cellular energy metabolism observed in aged animals. The accumulation of free radicals and the decrease of antioxidant systems could cause alteration of the oxidative phosphorylation mechanism.¹¹ This does not conflict with the mitochondrial DNA mutation theory because the beta subunit of ATP synthase is encoded by nuclear DNA.

MUTATION AND DAMAGE TO MITOCHONDRIAL DNA

The mitochondrial DNA (mtDNA), which resembles the circular bacterial DNA, only codes for about thirteen of the proteins that are found in the electron transport chain. The majority of the proteins, approximately sixty, are encoded from nuclear DNA. Both mtDNA and nuclear DNA are susceptible to mutations by oxygen free radicals. This can cause death or dysfunction of the mitochondria and eventual cell death by interfering with oxidative phosphorylation. Frequencies of mutations differ between mtDNA and nuclear DNA.

The occurrences of mtDNA mutations are much higher than nuclear DNA mutations. The levels of oxidative damage to mtDNA range from ten to seventeen times that in nuclear DNA, depending on the part of the body sampled. Shigenaga has been proposed that this is due to the mitochondrial association with oxygen.¹²

¹⁰ Kroll, J. 15 June 1996. "The ATPase Module and the Process of Cellular Imortilization." Annals of the New York Academy of Sciences. 768. : p.57-61.

¹¹ Guerrieri, F. Vendemiale, G. Turturro, N. Fratello, A. Furio, A. Muolo, L. November Grattaglino, I Papa, S. 15 June 1996. "Alteration of Mitochondrial F₀F₁ATP Synthase during Aging." Annals of the New York Academy of Sciences. 768: p62-71.

¹² Shigenaga, M.K. Hagen, T.M. Ames, B.N. 8 1994. "Oxidative damage and the mitochondrial decay in aging." Proceedings of the National Academy of Sciences of the United States of America. 91(23): p.10771-8.

Not only do mitochondria have a greater rate of mutation but they also lack DNA repair mechanisms. This means that through mitotic divisions, mitochondrial DNA mutations are likely to accumulate with age.¹³ (Stephenson, '96, p.1532).

MITOCHONDRIAL LIPID MEMBRANES AND ANTIOXIDANTS

Lipid membranes are also susceptible to oxidative damage over time. The fluidity of cellular and mitochondrial membranes decreases with age due in part to the changes in membrane compositions and lipid peroxidation. This will increase electrical resistance in the Schwann cell sheaths. The high electrical resistance in the Schwann cell sheath accounts for only one of the reasons that the electrical signals which are part of the neurological information transmitting process are diminished and the signal to the brain through the optic nerves is degraded.

A diphosphatidyl glycerol derivative in the mitochondria, called cardiolipin, performs many important roles in membrane structure and function. Among them, cardiolipin contributes to the control of permeability of the inner mitochondrial membrane to small molecules and helps maintain the electrochemical proton gradient. The sensitivity to oxidation increases with age and the amount of this valuable membrane compound supposedly decreases with age. This is paralleled by a decrease of the inner membrane surface area, and increased fragility of the mitochondria (Shigenaga, '94, p.10774-5).

A decrease in inner membrane surface decreases the cells' abilities to synthesize. Increased mitochondrial fragility will increase mitochondrial attrition. In both cases, ATP concentrations in the cells decrease.

Glutathione (GSH), an intracellular antioxidant agent, has been shown to protect the oxidative phosphorylation mechanisms from the ravaging effects of free radicals. This is done by the binding of the GSH molecule to the ATP synthase complex, which somehow protects them from unwanted oxidation.

Antioxidants, which can be found in foods, include ascorbate, tocopherols, and carotenoids. Evidence indicates that damage from aging ailments such as cancer, cardiovascular disease, and brain dysfunction can be avoided or at least minimized by dietary intake of fruits and vegetables that are high in antioxidants (Shigenaga, '94,p.10771).

¹³ Stephenson, J. 22 May 1996. "A Role for Mitochondria in Age-Related Disorders?" JAMA. 275(20): p.1531-2.

MITOCHONDRIA SECTION CONCLUSION

Since the mitochondria are the main energy producers of organisms, if they are not functioning properly, diseases are likely to occur. The coordinated interactions between antioxidants, ATP synthase, DNA, and the free radicals are in a delicate balance through the early portion of life and gradually go out of balance, causing disease by degradation of the mitochondria. This is what we see as the phenotype of aging.

The Relationships between ATP, Mitochondrial Function, and Visual Function

It is my belief that the complex of symptoms which together define the ARMD syndrome, are actually related because they are all sequelae of the body's deteriorating energy subsystem.

I believe that there are a number of metabolic factors that participate in the ARMD complex. Below I have listed four metabolic functions, each of which might be partially responsible for ARMD. Each one of them depends, to one degree or another, on the adequate availability of ATP.

After the listing of each metabolic task, I have briefly expressed the mechanisms by which treating the eyes with microcurrent should hypothetically improve visual acuity for ARMD patients.

Microcurrent affects ARMD by impacting the following functions:

- 1.) *Restoration of visual purple and rhodopsin after light reception and transmission has taken place.* -- How quickly the visual purple and rhodopsin can be restored after they are used to send or attempt to send a signal to the brain will affect future light sensing efficiency. As with any protein synthesis in the body, the synthesis of the visual pigments is an endothermic reaction that requires a supply of energy. ATP supplies the energy that the body uses for protein synthesis.
- 2.) Rebuilding the intracellular ATP concentration for neurological repolarization after the ATP has been depleted. -- After a nerve fires (depolarizes), assists in re-polarizing cell membrane potential. Supplies the energy that is needed when the cell removes metabolic waste and imports fresh metabolites using the active transport mechanism.
- 3.) Repolarization of the optic nerves. -- Adequate intracellular concentrations of ATP, which is produced in the Mitochondria, are essential for the optic nerve to transfer information to the brain after its fibers have been stimulated by the rods or cones. This [ATP] concentration will affect the functioning of the sodium pump and hence, affect the cell's ability to re-polarize (re-polarization

efficiency). More specifically, a completely re-polarized neuron will have a cell membrane potential of about -85 millivolts. When an action potential traverses the neuron, the cell membrane potential is reduced along the cell membrane. This reduction of the cell's polarization, which occurs as a wave of de-polarization, is the action potential. Hence, for the neuron to fire again, the cell membrane potential must be re-established.

- 4.) Enhancing the cell's waste management systems. -- Loss of the ability to process waste materials and re-polarize is a common finding in aged and ATP deficient cells in all parts of the body.

Hypothesis: I propose that what the MCS devices do is enhance the cell's ATP synthesizing capabilities. Theoretically, if each or any of the above scenarios are accurate and we actually have a technology that is capable of increasing cellular ATP concentration, specifically in the area of the eyes, we could provide the means to improve visual acuity for ARMD patients. The balance of this document is structured to support the presuppositions above.

ATP - Nature's Energy Store

All living things, plants and animals, require a continual supply of energy in order to function. The energy is used for all the processes that keep the organism alive. Some of these processes occur continuously, such as the metabolism of foods, the synthesis of large, biologically important molecules, e.g. proteins and DNA, and the transport of molecules and ions throughout the organism. Other processes occur only at certain times, such as muscle contraction and other cellular movements. Animals obtain their energy by oxidation of foods; plants do so by trapping the sunlight using chlorophyll. However, before the energy can be used, it is first transformed into a form that the organism can handle easily. This special carrier of energy is the molecule adenosine triphosphate, or ATP.

ATP METABOLISM AND SYNTHESIS UNDER THE INFLUENCE OF ELECTRICAL STIMULATION

The Different Metabolic Effects of Standard Millicurrent TENS VS Microcurrent.

Even though, historically, both microcurrent and TENS devices have tended to be classified as substantially equivalent to pre-amendment TENS devices, there appears to be a very elemental divergence between the biological effects of the two technologies. While at the upper(millicurrent) end of the TENS current spectrum, the electrical stimulation can block the neurological transmission of pain signals, there appears to be a dramatic difference in the metabolic effects at the lower end, the microcurrent end.

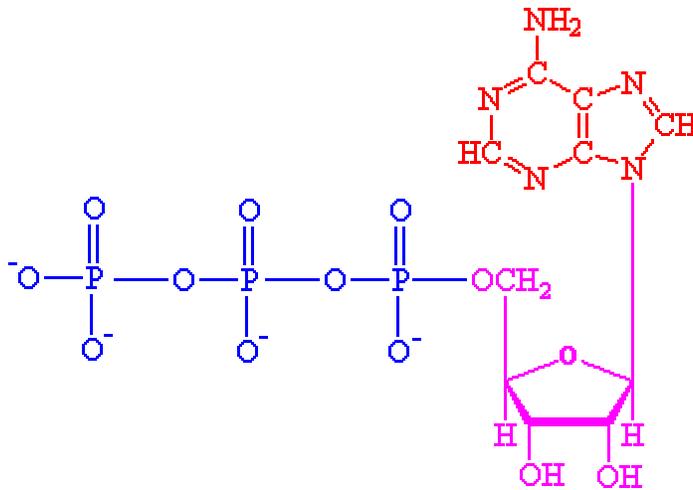
Research by Cheng Et. Al.¹⁴, demonstrated a very significant difference between the types of electrical stimulators known as TENS devices and those classified as MicroCurrent devices. Cheng demonstrated that currents in the range of about 200-750 microAmps tended to increase ATP concentrations in cells, while currents above 1 milliAmp tended to lower intracellular ATP concentrations.

Herein lies the quintessential difference between milli and microcurrent devices.

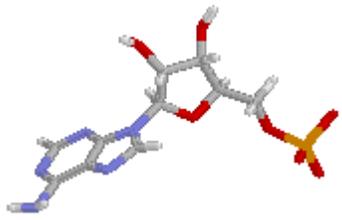
ATP Structure

The ATP molecule is composed of three components. At the center is a sugar molecule, ribose (the same sugar that forms the basis of DNA and RNA). Attached to one side of this is a base (a group consisting of linked rings of carbon and nitrogen atoms); in this case the base is adenine. The other side of the sugar is attached to a string of 3 phosphate groups. These phosphates are the keys to the activity of ATP. The three phosphates are linked together by high-energy bonds. When the high-energy bonds are broken, energy is released from the ATP molecule.

The ATP Molecule

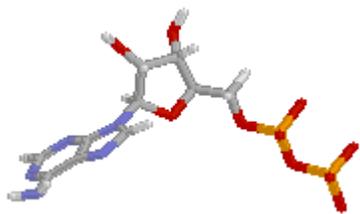
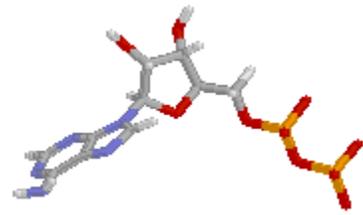


¹⁴ Cheng, Ngok, Et Al., November-December 1982. "The Effects of Electric Currents on ATP Generation, Protein Synthesis, and Membrane Transport in Rat Skin." , "Clinical Orthopedics and Related Research, 171, November-December 1982, pp.264-271



AMP

ADP



ATP

ATP Metabolism

ATP is adenosine triphosphate. It is synthesized in the mitochondria by the process that is known as the Krebs's Cycle, the sequence of reactions in the mitochondria that complete the oxidation of glucose in respiration. This process of cellular respiration uses oxygen and glucose and releases CO₂ as a byproduct. This endothermic reaction uses the enzyme, ATP synthase, to combine phosphate radical with ADP (adenosine diphosphate) plus electrons supplied by the breakdown of pyruvate and glucose to create a relatively unstable, high-energy molecule called ATP. It is the high energy and the instability of this molecule that makes it valuable and useful.

ATP works by losing the endmost phosphate group when instructed to do so by an enzyme. This reaction releases a lot of energy, 7 calories per gram, which the organism can then use to build proteins, contract muscles, etc. The reaction product is adenosine diphosphate (ADP), and the phosphate group either ends up as orthophosphate (HPO₄) or attached to another molecule (e.g. an alcohol). Even more energy can be extracted by removing a second phosphate group to produce adenosine monophosphate (AMP). This event is less common.

When the organism is resting and energy is not immediately needed, the reverse reaction takes place and the phosphate group is reattached to the molecule using energy obtained from food or sunlight. Thus the ATP molecule acts as a chemical 'battery', storing energy when it is not needed, but able to release it instantly when the organism requires it.

The body must constantly generate ATP. A male body uses 8000 grams of ATP per hour. A male body can only hold 100 grams of ATP at a time. ATP can release up to 14 calories per gram, but this requires breaking both phosphate bonds. Usually only one phosphate bond is broken, hence 7 calories of energy release per gram is the norm. It is crucial that the system, which produces ATP, be maintained for optimal performance because the equivalent of all the ATP in the body must be replaced 80 times per hour (every 45 seconds).

The Krebs's cycle is the respiratory cycle that is responsible for cell respiration, the manufacture of ATP, and the production of the waste product, CO₂. The main function of the mitochondria is the oxidation of the pyruvate derived from glycolysis and related processes to produce the ATP required to perform the cellular work. Free radicals, a type of highly reactive, destructive molecules, are a byproduct of this process and may be implicated in the aging process.

KNOWN GENETIC LINKS BETWEEN ATP AND RETINAL DYSFUNCTION

RP Connection

It is possible that ATP metabolism is one of the significant keys that may unlock the secrets of ARMD treatment. ATP Synthase, a.k.a. ATPase, is an enzyme that catalyzes the synthesis of ATP. A genetic defect in the ATPase 6 gene has been implicated in the disease Retinitis Pigmentosa (RP). RP has similarities to ARMD, not the least of which is that RP is a type of progressive retinal degeneration.

The mitochondrial genome (mtDNA) in humans is contained on a single circular chromosome 16,569 basepairs around, and each mitochondrion contains 5 to 10 copies of the mitochondrial chromosome. There are several essential genes in mtDNA that are involved in replication and translation, along with some genes that are crucial for the machinery that converts metabolic energy into ATP. These include NADH dehydrogenase, cytochrome c oxidase, ubiquinol/cytochrome c oxidoreductase, and ATP synthase, as well as the genes for unique Ribosomal RNA and Transfer RNA particles that are required for translating these genes into proteins.

There are specific diseases associated with mutations in some of these genes. Below is one of the affected genes and the disease which arises from its mutation.

Mutation of the ATP synthase gene:

Myoclonic Epilepsy and Ragged Red Fiber disease, MERRF, involves mutation of the ATPase 8 gene. While Neurogenic muscle weakness, Ataxia, and **Retinitis Pigmentosum (RP)**, NARP, results from mutations in the ATPase 6 gene.

RP is a genetically linked dysfunction of the retina and is related to mutation of the ATP Synthase Gene 6^{15, 16, 17}.

¹⁵ Molecular Biology of the Cell by Bruce Alberts, et al. - 3rd ed., Garland Publishing, Inc., New York & London, 1995.

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An Introduction to Genetic Analysis by Anthony J.F. Griffiths, et al. - 5th ed., W.H. Freeman and Company, New York, 1993

¹⁷ <http://128.252.223.112/posts/archives/mar98/890683118.Cb.r.html>

ARMD and ATP in Stargardt's disease ¹⁸

Stargardt's disease (STGD, also known as fundus flavimaculatus; FFM) is an autosomal recessive retinal disorder characterized by a juvenile-onset macular dystrophy, alterations of the peripheral retina, and subretinal deposition of lipofuscin-like material. A gene encoding an ATP-binding cassette (ABC) transporter was mapped to the 2-cM (centiMorgan) interval at 1p13-p21 previously shown by linkage analysis to harbour the STGD gene. This gene, ABCR, is expressed exclusively and at high levels in the retina, in rod but not cone photoreceptors, as detected by in situ hybridization. Mutational analysis of ABCR in STGD families revealed a total of 19 different mutations including homozygous mutations in two families with consanguineous parentage. These data indicate that ABCR is the causal gene of STGD/FFM.

¹⁸ Allikmets R, Singh N, Sun H, Shroyer NF, Hutchinson A, Chidambaram A, Gerrard B, Baird L, Stauffer D, Peiffer A, Rattner A, Smallwood P, Li Y, Anderson KL, Lewis RA, Nathans J, Leppert M, Dean M, Lupski JR, A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy., *Nat Genet* 1997 Mar;15(3):236-46

The Role of ATP in the Active Transport Mechanism

ATP increases the cell's ability to re-polarize because it provides the fuel that powers The Active Transport Mechanism

Active Transport

Active transport requires the expenditure of energy to transport a molecule from one side of the membrane to the other, but active transport is the only type of transport that can actually take molecules up their concentration gradient as well as down.

Similarly to facilitated transport, active transport is limited by the number of protein transporters present.

We are interested in two general categories of active transport, primary and secondary. Primary active transport involves using energy (usually through ATP hydrolysis) at the membrane protein itself to cause a conformational change that results in the transport of the molecule through the protein. The most well-known example of this is the Na⁺ K⁺ pump. The Na⁺ K⁺ pump is an antiport, it transports K⁺ into the cell and Na⁺ out of the cell at the same time, with the expenditure of ATP.

Secondary active transport involves using energy to establish a gradient across the cell membrane, and then utilizing that gradient to transport a molecule of interest up its concentration gradient. An example of this mechanism is as follows: *E. coli* establishes a proton (H⁺) gradient across the cell membrane by using energy to pump protons out of the cell. Then those protons are coupled to lactose at the lactose permease transmembrane protein. The lactose permease uses the energy of the proton moving down its concentration gradient to transport lactose into the cell. This coupled transport in the same direction across the cell membrane is known as a symport. *E. coli* uses similar proton driven symports to transport ribose, arabinose, and several amino acids.

The Na⁺ -glucose secondary transport mechanism

Another secondary active transport system uses the Na⁺-K⁺ pump as the first step, generating a strong Na⁺ gradient across the cell membrane. Then the glucose-Na⁺ symport protein uses that Na⁺ gradient to transport glucose into the cell.

This system is used in a novel way in human gut epithelial cells. These cells take in glucose and Na⁺ from the intestines and transport them through to the blood stream using the concerted actions of Na⁺-glucose symports, glucose permeases (a glucose facilitated diffusion protein), and Na⁺-K⁺ pumps. Note

that the epithelial cells are joined together by tight junctions to prevent anything from leaking through from the intestines to the blood stream without first being filtered by the epithelial cells.

Aging cells often experience a decrease in ATP concentration and then lose their ability to efficiently process metabolic waste. It is this deficiency which causes each of the active mechanisms to falter and causes the primary ATM (active transport mechanism) to malfunction.

What else does the ATP and the active transport mechanism do?

Let's talk about neurological signal transmission because this is the focus of my understanding why some retinas, even though infested with drusen, still function to allow the complete transmission of vision signal to the brain. There are at least two very important events that occur when a nerve sends a signal. One event is analog and the other is digital. Both events are required for complete and accurate information processing/ signal transmission.

When a nerve fires, a wave of depolarization moves along its body towards the next synapse. This wave is called an action potential. A polarized nerve cell is in a ready state, ready to fire, ready to de-polarize. A polarized cell has an abundance of sodium (Na^+) ions external to the cell membrane and an abundance of potassium (K^+) ions on the intra-cellular membrane.

De-polarization is characterized by the sudden movement of Na^+ into the cell in exchange for K^+ , which moves out of the cell. Although the nerve cell does not completely depolarize, its state of readiness is reduced. As a cell is further and further de-polarized, its response ability is further and further compromised.

In order for the nerve cell to reach its full potential, both literally and figuratively, its membrane must be re-polarized. The process by which the cell is re-polarized uses the energy that is provided by the breakdown of ATP. This process depletes ATP stores.

Re-polarization of the cell is an 'uphill' battle. Both sodium and potassium ions must be transported against their potential gradients. When a solute needs to move from an area of lower to an area of higher concentration, normal laws of diffusion can not compensate. The solute calls on a Protein "buddy" for help across the membrane. The energy used to fuel this transportation comes from ATP, a chemical energy. It is often necessary for these solutes to be transported to the areas of higher concentration for the cell to function.

The mechanism by which ions are moved against a concentration gradient is called the Active Transport Mechanism (ATM). The ATM is an electrochemical

reaction that occurs at the cell membrane. This process is the mechanism by which metabolic waste and excess Na^+ are actively removed from the cell and glucose and K^+ are moved into the cell's interior.

Re-polarization and Cellular Housekeeping

How does the cell rid itself of metabolic waste and bring in fresh metabolic substrate (glucose)?

To a great extent, ATP is responsible for the most important cellular metabolic functions. It is often called the cell's currency. At the cell membrane, ATP is broken down when activated by the enzymes present at the membrane. These enzymes catalyze ATP to break down to ADP (Adenosine diphosphate) and Phosphate radical, and release electrons. At this point the freed electrons provide the energy to combine certain proteins with the metabolic waste materials which are the breakdown products of cellular metabolism. **In the retina, this includes the protein wastes from the breakdown of retinal cellular pigments (discs).**

This electromolecular change causes the metabolic waste to become differentially permeable in material that forms the cell membrane. What this means is that these waste products suddenly are imbued with the ability to dissolve into the cell membrane, but only in one direction, out (hence, the meaning of differentially permeable). The direction of permeability may have electronic/magnetic polarity as one of the factors affecting the direction of permeability. There is also an effect at the cell membrane that is the result of an excess of protons, which creates an ion pump that actively removes unneeded molecular waste, such as protein byproducts, from the cell.

Once out of the cell, the metabolic waste products are released into the bloodstream. A similar reaction occurs with metabolic substrate (food/glucose in the bloodstream) located in the bloodstream outside the target cells. The extra-cellular metabolic substrate becomes permeable towards the inside of the cell. It dissolves into the cell membrane, differentially permeable now only in the direction of extra-cellular to intracellular, and delivers nutrition to the cell. This is part of the active transport mechanism that provides nutrition to the cells.¹⁹

¹⁹ <http://www.bris.ac.uk/Depts/Chemistry/MOTM/atp/atp1.htm>

The Far Reaching Importance of ATP Molecule Acknowledged in 1997 by the Nobel Prize Committee.

The 1997 Nobel Prize for Chemistry

The Nobel Prize for Chemistry in 1997 was shared by Dr John Walker of the Medical Research Council's Laboratory of Molecular Biology (LMB) at and Dr Paul Boyer of the University of California at Los Angeles and Dr Jens Skou of Aarhus University in Denmark.

The prize was for the determination of the detailed mechanism by which ATP shuttles energy. The enzyme that makes ATP is called ATP synthase, or ATPase, and sits on the mitochondria in animal cells and chloroplasts in plant cells.

Walker first determined the amino acid sequence of this enzyme, and then elaborated its 3 dimensional structure.

Boyer showed that contrary to the previously accepted belief, the energy requiring step in making ATP is not the synthesis from ADP and phosphate, but the initial binding of the ADP and the phosphate to the enzyme.

Skou was the first to show that this enzyme promoted ion transport through membranes, giving an explanation for nerve cell ion transport as well as fundamental properties of all living cells. He later showed that the phosphate group that is ripped from ATP binds to the enzyme directly. This enzyme is capable of transporting sodium ions when phosphorylated like this, but potassium ions when it is not. This is a key to the function of ATP in the Active Transport Mechanism.

The following is from the Nobel Site²⁰

Boyer has called ATP synthase a molecular machine. It may be compared to a water-driven hammer minting coins.

The F₀ part is the wheel, the flow of protons is the waterfall and the structural changes in F₁ lead to three coins in the ATP currency being minted for each turn of the wheel.

²⁰ <http://www.nobel.se/announcement-97/chemistry97.html>

NERVE CONDUCTION VELOCITY

The Possible Effect of Increased Nerve Conduction Velocity on Visual Acuity

The Fusion of Flickering Light by the Retina²¹

When a visual image or a flash of light reaches the retina, it excites the visual receptors for up to 1/10 second. Because of this persistence of excitation, rapidly successive flashes of light become fused together and give the appearance of being continuous. The action of a motion picture seems continuous even though we all know that the images are actually discontinuous, a series of rapidly changing still pictures. The images on the motion picture screen are flashed at the rate of 28 frames per second and that is more than enough to provide total fusion.

At low intensity, fusion can occur when the flicker rate is as low as 5 or 6 flashes per second, while in bright illumination the critical frequency for fusion can rise up as high as 60 flashes per second.

The sensitive portions of both the rods and cones contain light sensitive chemicals that decompose on exposure to light. The decomposition products in turn stimulate the cell membranes of the rods and cones, eliciting nerve impulses that are then transmitted into the nervous system and to the brain where they are interpreted as images.

The Relationship between Resolution and Neurological Refresh Rates (JSR)

Consider your computer monitor. A relatively high-resolution monitor will have approximately from 600 X 800 or 768 X 1024, to rarely more than 1920 X 1200 pixels. This is a pixel count of 480,000 to about 2.3 million pixels. That is pretty good.

In your macula, which is about 1 square millimeter in size, you have about 120 million rods and 7-8 million cones. Each rod and each cone is a pixel. At 128 million pixels, that is about 40 to nearly 300 times more pixels than a very high-resolution monitor. Even more amazing is the comparison of the real estate population density of the macular to the high res monitor. A 19 inch monitor has about 175 inches square, or 1131 cm² or 1.1 million square millimeters surface area. 1.131 million times more surface than the macula. And 1% of the number of pixels. The macula has a pixel surface density of about 100 million times greater than a high resolution monitor.

²¹ Guyton, Arthur C, Textbook of Medical Physiology., W.B.Saunders Chapter 50, 1967

A better comparison would be to the new CCD filmless cameras. The latest SONY CCD has a ½ inch (8.93 mm diagonal), 3.24 million pixel CCD (equivalent of the camera's retina). This is the highest resolution CCD currently available commercially in quantity. It produces very high quality photographs, adequate in quality for the cover of Life Magazine. Yet, it has only 2.5% of the pixels of the macula and it is about 30 times the size of the macula. This is an extrapolated density ratio of about 1:2500 (CCD:Macula). The macula is still the more remarkable technology by a factor of twenty-five hundred to one.

Consider your computer from 10 years ago: It had maybe 10 to 50% of the resolution of your current system. And you can see the difference. That is why you upgraded. Now you have more detail, faster refresh times, and shorter latencies. All of these details are critical for having the smoothest viewing.

Think about your ability to view video clips or AVI or quicktime clips a just a few years ago. Technology which was borderline pathetic is now coming of age. Images can now refresh at a rate that is allowing the flicker and tiny picture sizes of 1992 to yield to full screen, smooth action. Remember, flicker rates less than 24 frames per second could be noticeable as discontinuous in normal light.

Significance of Nerve Conduction Velocity

Remember that these signals are not only occurring up to 2500 times per second, they are also creating a residual effect in the brain that can last up to .1 second. Each signal is the equivalent of a pixel of information and the pixel resolution is increased as the number of signals per second to the brain is increased. The speed that a nerve transmits a signal is called nerve conduction velocity. More signals per second equals an increased nerve conduction velocity. Since the brain images holographically, individual 'pixels' can be transmitted serially and can overlay the previous signal, increasing the signal strength before the previous image fades.

Dr. Margaret Naeser is a research Professor of Neurology at Boston University School of Medicine. She has been the Principal Investigator on two studies using the MicroStim devices for the treatment of Carpal Tunnel Syndrome. In her study, Dr. Naeser presents evidence that MCS enhances nerve conduction velocity. In her study, Dr. Margaret Naesar uses MCS together with Low Level Laser.

In October 1999, Dr. Naeser presented a paper²² for the North American Laser Therapy Association. The presentation was made at the FDA Headquarters, Rockville MD. Table 3 of that presentation presents the Changes in Median Nerve Sensory Latency Times. Of the ten cases that were presented, only 7 could be evaluated because the pretreatment nerve conduction velocities could

²² Treatment of Carpal Tunnel Syndrome with Laser Acupuncture, Low Level Laser Therapy.

not be measured. The other 7 patients all showed measurable increases in nerve conduction velocity. The study showed that nerve conduction velocities were increased at a level of significance of .006. There was no significance to the changes in nerve conduction velocities following the sham treatments ($p=0.90$ (n.s.)).

Possible causes of decreases in nerve conduction velocities

Where are some of the possible retinal/optic nerve bottlenecks and how might MCS help to resolve them?

- 1.) Optic nerve bundle cells are present but not firing: Not enough ATP to effect rapid re-polarization of the cells. Stimulation increases ATP, which, in turn, increases the re-polarization rate. In many cases, cells, which were not re-polarizing at all and were so toxic as to be on the verge of death, could be metabolically cleansed and energetically boosted back into play.
- 2.) Not enough pixels: Rods and Cones and neurological receptors which are out of the game but still alive on the injured list could be energized and brought back into play.
- 3.) Pixels refresh too slowly: Boosted ATP concentrations will enhance the refresh rate. That is, if the nerve cells are able to re-establish the resting potential more rapidly, they can fire more times per second.
- 4.) Signal strength is insufficient - Decrease in electrical resistance in the Schwann cell sheaths allows greater signal transmission with small signal strength.
- 5.) Nerve fibers are damaged - Enhanced protein synthesis may help repair damaged fibers.
- 6.) Inadequate refresh rate for visual pigments - Maybe we can enhance refresh rates of visual pigments with MCS. Many patients have reported enhanced color perception.
- 7.) Inadequate concentrations of neurotransmitters - Once again - building blocks of the neurotransmitters rely on ATP for fuel.
- 8.) Ischemia: MicroCurrent provides smooth muscle relaxation in the walls of the local blood supply, decreases the blood pressure locally, and promotes enhanced oxygenation.
- 9.) Poor cellular nutrition: MCS enhances glycogen uptake, which is further facilitated by the more abundant blood supply.
- 10.) Poor analog signal strength
Becker has demonstrated that Acupuncture points are not simply points of high electrical conductivity but are actually analog signal amplification

stations. Using the MCS puts a charge on the tissue and increases the Acupuncture point's amplification abilities. In this way, more signal gets to the brain, even if the Schwann cell sheath resistance is constant. Add the additional advantage of reducing the resistance in the myelin sheath and you further enhance the amplification characteristics.

Age Related Neurological Slowdown

The ATP Connection

Vision is a reflex. As we age, our reflexes slow. Is it then so unusual that our vision “slows” as well?

I suggest that this degeneration occurs because our neurological efficiency is compromised by age. I suggest that we do not respond as quickly because there are simply not as many cells in any particular nerve bundle ready to fire at any given moment, not that we necessarily do not have as many cells. Simply that not as many as them are in the state of “Ready to Fire”. Why?

For one thing, as we age, ATP concentrations diminish. Mitochondrial concentrations per cell wane. Mitochondrial efficiency dissipates as free radical damage causes more and more mutation of mtDNA. Hence, if the primary molecule, ATP, which is responsible for the rapid re-polarization of each and every nerve fiber, is scarce, those cells will not re-polarize or will re-polarize slowly. ATP has been called the cell’s currency. We need to keep these cells rich (in their currency) and living in abundance.

In addition, what about the concentrations of ATP synthase, which is a protein molecule? ATP synthase is critical in the synthesis of ATP. Since microcurrent electrical stimulation is capable of enhancing the cell's ability to synthesize protein, possibly one of the proteins which is enhanced is ATP synthase, hence the concentrations of ATP itself could potentially be increased.

I believe that using the MCS on post surgical tissues and scars will increase the transmission of information through the area of pathology. I have seen dozens of patients treated who have reported a nearly immediate decrease in numbness (increase in sensation) in areas that had lost sensation subsequent to surgical procedures or trauma.

It appears that this treatment may enhance peripheral neurological competency. A study conducted at the Boston University School of Medicine by Dr. Margaret Naeser and presented to the FDA in 1998 showed that the MocoStim increased nerve conduction velocity in patients treated for Carpal Tunnel Syndrome. Why not see if we are able to do the same thing in the eye? The evaluation of optic nerve conduction velocity is the genesis point for another clinical trial, which will have to wait until after the initiation of the currently pending ARMD trials.

As we increase the ATP concentrations in the cells, the cell’s ability to create the cell membrane potential increases in direct proportion to the concentration of

membrane charge. That is why larger nerves tend to conduct faster than smaller ones, which have a smaller concentration of membrane charges.

Note: The cell, when sending an action potential, does not completely depolarize. Only a small amount of ion crosses the membrane. This is why hundreds of thousands of impulses can be transmitted even after a nerve has been removed from the body.²³

Action Potential and Nerve Conduction Velocity

The refractory period: A second action potential cannot occur in an excitable fiber as long as that fiber is still depolarized from the previous action potential. This is called the absolute refractory period. The absolute refractory period of a large myelinated nerve fiber is 1/2500 second. Therefore, one could calculate that such a fiber could carry a maximum of 2500 impulses per second. This period is followed by a short period of super-excitability. (Guyton)

Consider what the MCS is designed to do, create an electrical charge on tissue. Using this device to enhance the membrane charge on the optic nerve might have the effect of increasing the concentration of charge on the cell membrane. It will, simultaneously, decrease the electrical resistance on the cell membrane, increasing the flow of the current named the current of injury by R.O.Becker MD.²⁴

The greater the numbers of charges on the cell membrane, the faster it will conduct signals and hence, the greater the number of visual signals it could transmit per second. The brain interprets visual intensity and resolution by both the number and quality of the specific nerve fibers that are delivering information to the visual center. The faster conduction velocities which can be obtained by the more highly charged fibers will then permit more signals to be processed in a given period of time, giving rise to a higher resolution which equals better sight.

ENHANCING RESOLUTION

Hypothetically, what does it take to improve visual acuity?

- 1 Increase the number of functioning Rods and Cones in the Macula.
- 2 Increase the speed of re-polarization of the fibers of the optic nerve.
- 3 Increase the rate of regeneration of the Visual Pigments.
- 4 Enhance the blood supply to the macula.
- 5 Increase cellular nutrition.
- 6 Boost signal strength and/or decrease resistance to signal transmission.

²³ Guyton, Arthur C, *Textbook of Medical Physiology*, W.B.Saunders, 1967

²⁴ R. O. Becker, "The significance of bioelectric potentials," *Bioelectrochem. Bioenerg.*, 1, 187(1974).

- 7 Increase the concentrations and refresh rates of the visual neurotransmitters.
- 8 Increase optic nerve conduction velocity.

How these all add up. : The more clean signal that gets to the brain per unit of time, the higher the signal to noise ratio of visual information. The ways that the signal can be boosted are:

- 1) increased nerve conduction velocity = more signals per second = more frames per second = less flicker.
- 2) Lower Schwann Cell Membrane resistance = greater amplitude of the arriving analog current signal. This increases signal to noise ratio and delivers more and cleaner signals to the brain.
- 3) Decreased toxicity of the rods and cones = more individual signals transmitting information. Etc. That is, every change which increases the amplitude, clarity, and speed of transmission increases the resolution of the perceived signal.

Are all of these functions enhanced by MCS stimulation?

It's too soon to say, but I believe that most, if not all, of the above hypothetical means of increasing visual function can eventually be attributed to microcurrent stimulation.

The analog event: Most of the nerve cells (other than satellite and glial cells) are myelinated. This means that they are surrounded by a material that is lipoid (fatty) by nature and covers the whole body of the cell. This material is called myelin. Myelin is the main ingredient of the structure surrounding almost every nerve cell that is known as the Schwann cell sheath.

When I was in school, I was taught that the Schwann cell Sheath's only purpose was the isolation (insulation) of one nerve cell from another. Robert O. Becker MD, demonstrated that there is at least one more very important function, an information transmission conduit.²⁵ There is a measurable analog signal (a small DC current) which flows through each Schwann Cell Sheath. Working with rat bone fractures and surgically severed nerves, Dr. Becker demonstrated that this signal carries information which can direct the healing process and carry RNA coding to different parts of the body to guide and direct the healing process.

MS patients demonstrate the devastating effects of the loss of myelin sheath. This would happen, of course, if the insulation broke down, but the effects are much more complex than that. These sheaths carry the information that guides

²⁵ R. O. Becker, "The significance of bioelectric potentials," *Bioelectrochem. Bioenerg.*, 1, 187(1974).

the healing and many other functions of the body.²⁶ My experience has been that MS patients respond only minimally to microcurrent stimulation.

It is possible for electrical resistance to build up in the Schwann Cell Sheaths and block the transmission of the analog signal, which is a very tiny dc current. In the presence of excess resistance, the signal cannot make the entire trip from the input to the brain. I need more information about whether or not Drusen is present in the myelin sheath, but if it is, drusen, of course, has a higher resistance than the myelin which is designed to carry the signal and hence would slow down the transmission of information.

The more commonly accepted transmission method in the nervous system is via a wave of depolarization of the nerve cell membrane, which is known as an action potential. What depolarizes? There is a **concentration gradient** across the cell membrane which consists primarily of an excess of Na⁺ ion outside the cell and an excess of K⁺ ion inside the cell. There is also some interference of the movement of these ions by calcium ion at the cell membrane. Since the depolarization of a nerve either occurs or it does not, this is considered to be an all or nothing, or a digital signal.

The concentration gradient is created by the active transport of sodium out of the cell and potassium into the cell with energy supplied by the ATP breakdown reaction at the cell membrane. When there is more of an ion on one side of a semi-permeable membrane, this is known as a concentration gradient. The active movement of the two ions in opposite directions to create a concentration gradient takes time and energy. It is called re-polarization. The more ATP is present to do the work, the shorter the re-polarization time is.

The period of re-polarization is called the refractory period and is further divided into the absolute refractory and the relative refractory phases of re-polarization. During the absolute refractory phase, the nerve cell is re-polarizing, but has not reached the state where the nerve can fire (resting potential). It is **ABSOLUTELY REFRACTORY** to firing no matter how intense the stimulus. If there is not adequate energy in the cell, (i.e. not enough ionic concentration gradient), to move past the absolute refractory phase, the nerve will not fire. It will not carry any signal to or from the brain.

The absolute refractory (AR) stage is followed by the relative refractory (RR) stage. During the relative refractory stage, the cell will fire, but a larger than normal stimulus must be applied to create the action potential. If there is not enough ATP in the specific optic nerve for the cell to reach the full resting potential rapidly, it may not fire in the presence of normal light. Hence, if there is a deficiency of internal ATP in the optic nerve, many of the optic nerve bundle fibers will remain in either the absolute or relative refractory state, (the number of

²⁶ R. O. Becker, "The significance of bioelectric potentials," Bioelectrochem. Bioenerg., 1, 187(1974).

photons equals the intensity of stimulation) so the patient might be able to read in very bright light because the increased intensity of the stimulation overcomes the relative refractory condition and evokes an action potential.

I believe that we can treat the disease at this junction. If MCS increases the concentration of ATP in the optic nerve fibers, this increases the speed at which the cells can reach the state of complete readiness (a resting potential). It also increases overall the number of cells that are capable of reaching this ready state at any given moment. Hence, if we have more fibers ready to accept a signal at any given time and they are able to get back to this ready state more quickly, we have a more competent retina or more competent optic nerve, capable of sending more signal with less information. Hence, better vision.

As time moves on and the disease (ARMD) progresses and becomes increasingly chronic and degenerative, more cells enter, but fewer emerge from the relative refractory state. Hence, larger and larger luminosity is required for the patient to maintain status quo of visual acuity. Loss of night vision is an example of this phenomenon. Time moves on, more and more optic nerve fibers remain in the absolutely refractory state. These cells will not fire, no matter how bright the light and the neurons never leave the absolute refractory state - then absolute central field blindness ensues.

The lower the intracellular [ATP] (concentration of ATP), the more slowly the nerve fibers will pass through the refractory stages into the resting potential state and the smaller the number (percentage) of cells which is available to transmit information at any given moment. Conversely, an adequate intracellular [ATP] will provide a resting potential state most rapidly, enhancing vision by transmitting more data, more rapidly and hence allowing better perception with less magnification and in lower light. There are estimated to be about 1.5 million nerve cells in the optic nerve. Of these, nearly one million are in the macula, the more of these cells which can be kept in the ready state, the better will be the vision at any given luminosity.

Drusen

Where do you suppose drusen comes from, why is it there, and why is it generally age related?

This hyaline material (Drusen) is apparently made up of at least 11 different proteins²⁷

I propose that Drusen is an accumulation of intracellular garbage, mostly proteins, including the various breakdown products from the retinal pigments.

²⁷ Center for the Study of Macular Degeneration (CSMD)

These waste products precipitate and aggregate from cellular solution when the individual proteins and proteinaceous residue becomes hyper-concentrated in solution in the cell because of the cell's inability to take out the trash. Poor housekeeping, because of inadequate available resources results, in an unmanageable concentration of intra-cellular protein byproducts.

Remember that ATP concentration must be adequate to provide the energy at the cell membrane to create the differential permeability necessary to move the waste products out of the cell. It has been postulated that there is an auto-immune response at work here. I propose that if there is an autoimmune response, it results from and is not the cause of this accumulation of antigenic material. These protein byproducts needed to be properly flushed from cells, which had produced them in the normal course of events.

The math is quite simple. Each cell holds an electrical charge and is electrically polarized. A body cell, like a battery, when it has no charge, is dead. An inadequately charged cell cannot manufacture ATP. A cell deficient in ATP can not rid itself of metabolic waste. A nerve cell deficient in ATP cannot re-establish membrane potential and hence cannot fire or fires only when stimulated with an abnormally high signal. A nerve cell deficient in ATP will have a decreased nerve conduction velocity.

The life of every cell is dynamic. Proteins and inclusion bodies are constantly being created, dismantled, used up, and (hopefully) cleaned out and replaced. If there is a breakdown in any part of this process, the cell ages. By this, I mean, the cell becomes less vibrant and less responsive to its environment and less capable of re-establishing its optimal equilibrium state. A cell that is able to continually re-establish optimal performance ages only chronologically. Physical aging is simply the loss of optimum vitality of any cell of the body.

With an aged cell, as the concentration of protein by-products builds up in solution in the cells. These concentrations may eventually reach the point of full saturation. One molecule past full saturation initiates precipitation. This is similar to the manner in which rock candy is made. When hot water is super-saturated with sugar and then cooled, the sugar crystals precipitate out of solution. Raising the temperature of the water or adding more hot water will change the concentration and allow the sugar back into solution. There may be a correlation to the drusen mechanism here that will bear looking at in the future. I have done some informal evaluation of the effect of microcurrent on tissue temperatures. Using a device called an infrared thermograph, I have observed that tissue temperature drops in tissues that are inflamed and increases in tissues that are deficient (cold or degenerative) when treated with microcurrent. Since the retina is in a degenerative state, the increased blood supply to the retina might increase retinal temperature and allow drusen to move back into solution. The increased energetic competence of the cell membrane transport mechanism could then move the drusen out of the cells, lowering the cellular

concentration of waste product and opening up the equation to allow more drusen to go into solution and be purged. This is highly speculative at this time, but is worth looking at.

Interestingly, there are people with large deposits of retinal head of drusen who still maintain good vision. This means that the presence of drusen, of and by itself, is not the ultimate deciding factor that necessarily determines diminished vision. It may be either an indicator or participant in the vision diminution, but it can not carry out the crime without an accomplice. Remember, though, that ARMD is a degenerative process. The macula can degenerate to the point that some, many, or all of the cells die. Once dead, there is nothing MCS can do for these cells. That is why many patients will show only initial improvement and eventually reach a plateau, beyond which additional improvement will probably not occur. What I am saying is that by re-establishing the cell's electronic competence and ATP concentrations, you can restore or maintain visual acuity in patients who have lost some or much of their vision.

I also propose that the prophylactic treatment of anyone predisposed to the disease would likely prevent the disease from ever developing. We would have the equivalent of an electronic vaccine for ARMD. I propose that at some future date, we may find that ARMD can be prevented, but that is the premise for another much longer study.

Molecular composition of drusen²⁸.

Using over 110 antibodies to a variety of extracellular matrix-specific molecules, researchers screened over 1,100 pairs of human donor eyes for evidence of drusen immunoreactivity. The screening resulted in the identification of at least eleven different molecules that are thought to be primary molecular constituents of drusen. These constituents are proteins that, heretofore, have not been implicated in ARMD or in any other retinal disease. In addition, the sequence of molecular events leading to drusen deposition has been partially characterized. Based on the known identities and functions of these drusen-associated molecules, it now appears that drusen formation is analogous to accumulations of extracellular matrix material in other prevalent plaque-forming, age-related disorders such as elastosis and atherosclerosis. This likelihood is supported by the epidemiological evidence indicating that these diseases are also risk factors for the development of ARMD.

MCS boosts cellular housecleaning mechanisms.

Proper application of electronic stimulation could have the effect increasing glycogen uptake in the cells of the macula /optic nerve/rpe layer of the retina. This, in turn, would increase APT concentrations which would then strengthen the nerve's conductance capabilities by re-establishing cellular membrane

²⁸ Center for the Study of Macular Degeneration (CSMD)

potentials to the -85 mV and increase the cellular membrane charge concentration required at the cell membrane for each cell to be in the ready state to fire normally and have an action potential evoked by a normal intensity of stimulation and operate with maximum nerve conduction velocity. A patient could read in normal light with all the nerve fibers in a state of near instant readiness. With adequate housecleaning mechanisms in place, drusen would not form or, if already formed, it would not continue to precipitate and accumulate because the concentration of protein waste products in the cells would not be adequate to create precipitation.

MCS aids the analog nerve grid.

There is that one more, very important aspect of the treatment. The MCS devices are designed to respond to the electrical resistance present in the treated tissue. Some of the more sophisticated MCS devices, like the MicroStim 400, even measure the degree of electrical resistance in an area of pathology. These devices increase and decrease their own electronic current and voltage outputs to finesse the highest possible electronic charge onto the tissue at the treatment location. The clinical version of the device, The Model 5M (common name MicroStim 400-III) will measure and provide the therapist with the location of the highest or lowest electrical resistance and guide the therapist to add stimulation to the tissue which needs it the most. This will effectively decrease the resistance in the tissue (including that of the myelin material of the Schwann Cell Sheaths) and enhance transmission of via analog information grid. This occurs in two ways simultaneously: By increasing the charge on the cell membrane the resistance to the conductance of the current of injury is decreased, hence effectively boosting the current of injury transmission efficiency and by boosting the nerve conductance.

Economic Considerations:

ARMD currently affects an estimated 15 million Americans. Because of the baby boomers, the number of Americans affected by this disease will probably double to triple in the next ten to fifteen years. Estimates, in the US alone, are that there will be 30 million affected by the year 2010. The cost to society of the loss of independence of our senior members cannot be measured by sheer dollars.

Theoretical benefits of MCS treatment for ARMD.

1. Increases ATP concentrations in the cells, providing the energy needed to create a normal cellular membrane potential for creation of action potentials. This facilitates the digital nerve net and allows more fibers in the optic bundle to be ready to transmit information at any given moment.
2. Increases ATP concentrations so that the cell has the energy available which is needed to fuel the active transport mechanisms and remove the metabolic waste in exchange for the glucose and nutrients. This might effectively prevent the further accumulation of drusen.
3. Increases intracellular glucose concentration so that the cell has adequate nutrition.
4. Increases intracellular protein synthesis so the cell has enhanced regenerative capabilities.
5. Decreases cellular electrical resistance and facilitates the analog nerve net.
6. Increases nerve conduction velocity.

7. Relax smooth muscle of the vessels of the retina, normalizing retinal circulatory supply. It is possible that we will find that the neovascularization which occurs when ARMD goes wet, is actually the eye's normal response to the poor circulation which occurs when local vessels are occluded. Vessel occlusion commonly leads to the proliferation of collateral circulation. That could be what we see when the retina neovascularizes. Possibly, if MCS decreases the level of vascular occlusion in the retina, we will see benefits to treat the wet form of the disease.

Conclusions of Scientific Rationale

Studies done by Cheng²⁹, et.al., have demonstrated that introduction of a constant current in the microcurrent range will have several important effects including:

- 1.) Increasing ATP concentration ([ATP]) up to 500% at the 500 microAmps range.
- 2.) Increasing glycogen uptake (the building blocks of ATP) and
- 3.) Increasing intracellular protein synthesis (enhancement of regenerative and healing abilities)
- 4.) Increasing nerve cell membrane potentials and nerve conduction velocities.

What if Cheng is right? What if we can increase the [ATP] in the optic nerve bundle, increase the percent of fibers in the resting state, optimally ready to fire, at any given moment. What if we can increase the intracellular glucose concentration to a normal level in starving cells by the simple application of a precise electronic current from the MicroStim®? What might happen? The active transport mechanism would function normally. Metabolic waste would be removed from the cell as it developed. Abundance of metabolic substrates would enhance intracellular protein synthesis. RPE cells might have no reason to develop drusen. The optic nerve bundle fibers would reach the resting state almost instantly after producing an action potential, and the vision would be normal or could be maintained at status quo for many years.

Most important is the effect Cheng has demonstrated that microcurrents have on ATP production. If ARMD is actually a disease of ATP metabolic deficiency, then it should logically follow that an intervention at the level of enhancing ATP synthesis would interrupt the cycle of the syndrome. The result would be that vision would be enhanced because of the increased vitality of the optic nerve, the RPE, the local circulation, and the retinal cells in general.

²⁹ Cheng, Ngok, Et Al., November-December 1982. "The Effects of Electric Currents on ATP Generation, Protein Synthesis, and Membrane Transport in Rat Skin." , "Clinical Orthopedics and Related Research, 171, November-December 1982, pp.264-271