



NuroKor[®]
BioElectronics

Physiological Mechanisms of MCS

Mediated Pain Relief and other Benefits

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Executive summary

Bioelectricity is embedded in the fabric of life and plays a vital role for normal physiological functions, regeneration, repair, healing and health across many species. Alteration in normal bioelectrical potentials is associated with disease and impaired ability to repair and heal.

Pain and inflammation can result from injury or disease, and are part of the body's defence mechanism, enabling it to respond to avoid further damage and initiate the healing process. However, it is essential to treat pain and inflammation promptly, because they can have devastating effects if left unchecked.

Microcurrent stimulation (MCS) represents one modality or version of electrotherapy, characterised by an amperage that closely emulates that of endogenous (internal) bioelectricity. The benefits of MCS have been investigated for several years, and research has shown that MCS is effective at alleviating pain.

The analgesic effects of MCS can be attributed to its ability to stimulate physiology, increase energy production and protein synthesis, augment the transport of nutrients and metabolites across the plasma membrane, and also increase blood flow, re-establish normal bioelectrical activity, reduce inflammation and combat infection. All these important factors promote cellular health, re-establishing tissue homeostasis, facilitating healing and repair, and consequently helping resolve pain.

At NuroKor, we produce multimodal, evidence-based electrotherapy technology that incorporates various formulations, including MCS.

The role of bioelectricity in living organisms

Research has revealed that the bioelectrical potentials within many species are an essential part of the physiological processes that sustain life. The studies, conducted by Burr et al., showed that bioelectric potentials exist in various organisms, including invertebrates, amphibians, humans and other mammals.

The bioelectrical currents occurring in living organisms are extremely small, while the bioelectrical system appears to have a specific geometrical configuration in different species, and the bioelectrical potentials are characterised by dynamic changes, exhibiting variations according to the level of physical activity.

Beyond physical activity, the seminal work of Becker and colleagues demonstrated that a bioelectrical response to injury exists within animals. This response to injury exhibits specific patterns that are dynamic in nature, which manifest soon after injury, and vary during the different stages of the healing process. Some species of vertebrates, such as salamanders, exhibit a high level of regenerating ability, and are able to regrow body parts, including entire limbs. Experiments on frogs and salamanders revealed that the pattern of bioelectrical current variation is different between animals able to just repair and animals able to regenerate. This difference in variation of bioelectrical potentials probably reflects the fact that repair and regeneration are two considerably different phenomena.

Although complex organisms such as vertebrates, including humans, have a large variety of cell types, from a bioelectrical point of view they can be broadly categorised into excitable cells, such as neurons and myocytes, and non-excitable cells that comprise all other cell types. These two types of cells function by utilising two types of bioelectrical potentials.

For instance, the activation of neurons involves the depolarisation of the plasma membrane, which is achieved by a flow of ions in and out of the nerve cell. Similarly, there are direct current (DC) potentials within glial cells, which are semiconducting in nature. Because neurons and glial cells are widely distributed, they can reach into all areas of the body to create a normal electrical environment around each cell.

These ionic and DC potentials are embedded within living organisms, exhibit a multi-layered arrangement, and are part of the endogenous bioelectrical system. The findings from several other studies conducted over the decades, suggest that bioelectrical potentials are involved in all aspects of life, across species, including normal physiological function, development, regeneration, growth, health status, healing, and level of activity.

From all these studies, it also emerged that the endogenous bioelectrical system is complex, with a macro-geometry that pervades the body architecture at different levels. There is also a micro-geometry, which is present in the cells' interior volume, across their membranes and those of the cells' organelles, as well as in the extracellular volume.

However, alterations of normal bioelectrical activity are associated with compromised function and disease. Tissue injury and disease are often associated with the inflammatory response and pain.

Pain and inflammation

Pain is an unpleasant physical and emotional sensation, which provides the central nervous system with a rapid warning about actual or potential tissue damage.

It is a very complex phenomenon, and its variability reflects intricate and dynamic neurophysiological processes. These involve the input of pain receptors from the peripheral areas of the body and its transmission to the cerebral areas, where the pain information is then processed and interpreted.

Pain is an essential component of the body's defence system, which enables it to initiate a motor response to minimise physical harm, and a physiological response to heal the tissues damaged. Moreover, tissue injury is associated with the inflammatory response leading to the development of inflammation.

In the absence of inflammation, usually when pain receptors are activated by an external stimulus, the pain sensation normally reflects the intensity of that specific stimulus. However, when inflammation does occur, pain can arise with minimal stimulation or even without an external trigger.

Inflammation represents an immune response to injury or infection, and the inflamed tissue is characterised by pain, oedema (swelling), heat and redness. The development of inflammation involves a series of physiological mechanisms aimed at defending the body from potential pathogens or foreign substances, and also activating the healing process.

Even though pain and inflammation are part of the body's defence mechanism, it is essential to manage them appropriately because they can have devastating physical, psychological and emotional consequences when unchecked.

Microcurrent stimulation (MCS) represents one of the electrotherapy modalities, which brings about a number of benefits, including improving pain and inflammation.

MCS is effective in mediating pain relief

MCS is capable of bringing about favourable physiological changes, which are conducive to health and also promoting tissue healing and repair. Moreover, there is evidence to suggest that MCS is also effective in relieving pain from different conditions. The current delivered during MCS treatments is characterised by an amplitude in millionths of an ampere range (μA). MCS therapy is based on the evidence that micro amperage currents closely approximate the endogenous current, which is generated naturally by the body's bioelectrical system.

One well documented source of pain, including lower back pain (LBP) is caused by myofascial trigger points. These are often in the form of knots or nodules that can be felt on the muscles beneath the skin and are usually described as micro-cramps. Myofascial pain can be debilitating; decreasing mobility and often impairing neurological, circulatory and lymphatic functions.

Myofascial LBP is difficult to treat, and is generally resistant to conventional therapy. A study evaluated the effect of MCS on myofascial chronic LBP in patients who had previously received standard treatments with minimal benefits. The patients included in the study received on average 6 MCS treatments over 6 weeks. The results showed that MCS application produced palpable changes within the tissue and alleviated pain, and these effects persisted long-term.

Lateral epicondylitis, also known as tennis elbow, is a tendinopathy of the arm muscles, and the pathophysiology of this condition is related to an overuse injury that also results in microtearing of various forearm muscles. The first stage of this condition involves the development of inflammation that leads to the formation of granulation tissue and adhesions at the site of the tear. The typical symptoms include tenderness and pain when touched around the lateral epicondyle and extensor muscles tendon origin. Other symptoms include pain associated with wrist and gripping motions, as well as decreased function and reduced grip strength. Research has shown that MCS application in patients with lateral epicondylitis helps improve pain, disability and grip strength.

Lumbar radiculopathy (pinching of a nerve root in the spinal column) is considered a serious health problem worldwide and symptoms can include pain, numbness and weakness of the gluteus muscles and leg - limiting function and affecting quality of life. A recent study has demonstrated that MCS application is effective in relieving pain, reducing inflammation, improving functional disability and nerve function in patients with lumbar radiculopathy. The authors concluded that MCS therapy could be recommended for the treatment of lumbar radiculopathy.

Other studies have shown that MCS application is effective in alleviating pain. MCS derived analgesia and the other health benefits result from a number of favourable physiological changes.

Physiological mechanisms of MCS mediated pain relief

Experimental findings suggest that MCS application mediates a number of benefits. These benefits, including pain management, can be attributed to the MCS derived effects that counteract the pathophysiological changes occurring within the traumatised or dysfunctional tissue.

Trauma or dysfunction impairs the bioelectrical potentials of the affected cells, and many of the benefits of MCS are mediated through the restoration of such bioelectrical potentials. In the affected cells, there is a reduction in adenosine triphosphate (ATP), as well as a disruption of the sodium-potassium pump, which are essential processes.

Moreover, compared with healthy tissue, the affected tissue is characterised by a higher electrical resistance. As a result, the electrical conductance and tissue capacitance are decreased, thereby hindering the flow of endogenous bioelectrical current. This contributes to impairing the healing process and also leading to inflammation. Similarly, the reduced membrane transport diminishes metabolites and nutrient influx into the cell, as well as waste product removal. All these changes impair normal function, and also are conducive to the development of pain.

MCS application to the dysfunctional or injured tissue emulates the body's endogenous bioelectrical current, which helps augment ATP synthesis and membrane active transport, which are important to re-establish normal tissue function, healing and addressing pain.

Bioenergetics

Bioenergetics focuses on how cells transform, store and utilise energy to power the myriad of life-sustaining biological processes. The energy extracted from substrates, such as carbohydrates or fat, is not utilised directly to power biological work, instead is used to resynthesize ATP.

These metabolic processes are vital, as ATP is one of the most important compounds of all living organisms, including humans, as it represents the energy currency to power all physiological processes required to sustain life. The body

breaks down ATP constantly and the energy it releases is utilised to power cellular functions, tissue healing and replenishment, nerve transmission, muscle contraction, growth, protein synthesis, digestion and glands secretion. Because of all these reasons, resynthesizing ATP is vital.

All tissues of the human body require a constant supply of ATP to sustain their physiological functions, and maintain their integrity. The body also needs to maintain optimal bioelectrical potentials through an appropriate concentration of ions, which involves influx and efflux of ions within each cell. ATP plays a vital role in achieving this by fuelling the active transport of ions, such as the sodium pump and potassium pump across the semipermeable membrane of all cells. In some cases due to health conditions, injury, high level of toxic substances or other factors, ATP synthesis declines. If adequate ATP synthesis is not re-established promptly, energy levels decrease, which compromises the normal cellular physiological functions and the efficiency of the ion pumps, with negative consequences on cells and tissues health.

There is evidence to suggest that the MCS application increases ATP synthesis in mammalian skin. The increased synthesis of ATP is the result of an MCS mediated proton gradient that is created across the functional membrane. Essentially, the microcurrent reacts with water (H_2O) to form protons (H^+) and ions (OH^-). This acid/base transition creates a gradient across the membrane. When the protons H^+ migrate and reach the mitochondrial membrane, they bind to the membrane-bound enzyme ATPase, resulting in ATP synthesis. These processes are to an extent similar to those occurring naturally during oxidative phosphorylation. Such processes are described in the chemiosmotic theory, developed by the British biochemist Peter Mitchell, who was awarded the Nobel Prize in 1978.

Transport of substances across the plasma membrane

All cells are separated from their surrounding environment by a semipermeable membrane, called the plasma membrane. The plasma membrane acts as a barrier regulating the influx of substances and metabolites into the cells, as well as the removal of waste products from the cells. The actions of specific transport proteins, which are present on the plasma membrane, mediate the movements of these substances in and out of the cells. These substances and nutrients include amino acids, pyruvate, ions, nucleotides and glucose, which are vital for maintaining physiological functions and cellular health.

Transport proteins are also involved in biological electrochemical processes such as neurotransmission. If the transport across the plasma membrane is not maintained optimally, the cells are starved of essential nutrients and metabolites. As a result,

physiological functions are compromised and waste products accumulate to a toxic level with potentially devastating consequences.

It has been shown that MCS application in mammalian skin re-establishes the nerve cell membrane potential to healthy levels, and reduces intracellular metabolic waste. This also allows new metabolites to enter the exhausted cell, therefore facilitating the regenerative functions to be re-established.

Amino acids transport, protein anabolism, and other MCS derived benefits

Protein metabolism is a critical process by which various types of protein are formed. After water, proteins are the most abundant substance present in cells, and typically constitute 10% to 20% of the total cell mass. Proteins are relatively large molecules and represent the building blocks of life. Proteins, in turn, are made up of many amino acids joined together to form long chains, much like beads arranged on a string.

Proteins can be broadly categorised into structural proteins, such as collagen and elastin, and functional proteins such as enzymes, antibodies, haemoglobin, neurotransmitters, hormones and so on. Proteins accumulate damage during their functional life, requiring constant repair and renewal via protein synthesis; this process is termed protein turnover.

Protein synthesis has an impact on all aspects of cellular life, as this process provides cells with structural and regulatory molecules necessary for cellular function and survival. The body uses a large part of its energy for synthesising proteins, and, in the optimal conditions, the body is capable of constantly producing new proteins to replace those damaged. However, this process is highly sensitive to the physiological state of the cell and the environmental conditions.

During tissue damage by injury or disease, it is essential to maintain adequate protein synthesis in order to sustain cell repair and renewal. Additionally, stimulation of protein synthesis increases the lifespan of different organisms. Studies have shown that MCS application in mammalian skin increases both amino acids transport across the cell membrane and protein synthesis. Furthermore, it has been found that MCS administration increases protein synthesis in mature nucleated amphibian erythrocytes.

MCS application to damaged and dysfunctional tissue augments ATP synthesis and membrane active transport, thereby permitting the intercellular influx of nutrients and metabolites, as well as the efflux of waste products out of the cell. The increased intracellular ATP and amino acids provide both the energy and the building material to synthesise new proteins to replace those damaged. Furthermore, the augmented energy availability sustains the cellular activity that helps re-establish homeostasis.

As the condition of the tissue improves, electric resistance is reduced and normal capacitance is restored, which permits the endogenous bioelectrical current to flow through the tissue normally, thereby re-establishing normal physiological function and allowing the emergence of healthy cells, promoting healing and tissue health.

In addition to mediating these favourable physiological changes, it has been shown that MCS application reduces prostaglandins and the release of other inflammatory mediators, thereby helping to reduce inflammatory reactions.

Alongside this, blood flow is a vital and essential factor that can affect the whole body organs and systems. However, muscular spasm, occurring as a reaction to trauma, causes a reduction in blood supply, resulting in local hypoxia, accumulation of noxious metabolites, and pain. Research has shown that MCS application improves blood flow. This increased blood flow augments oxygen, nutrients and metabolite delivery to cells and tissues, and also facilitates the removal of debris and waste products. Also, blood flow is an important factor that can affect the repair and healing of injured tissues.

All together, therefore, MCS application promotes ATP and protein synthesis, increases blood flow and improves inflammation. All these factors promote normal function and tissue repair, and the combined effects also address pain. The enhancement of tissue function and repair, mediated by MCS, is further supported by the findings from several studies, which demonstrated that MC therapy promotes wound and ulcer healing, as well as combating infection.

Effects of MCS on Skin Repair and Wound Healing

The skin is the tissue most at risk of wounds, which are often caused by impacts and also can result from surgery. Wound healing involves complex and dynamic physiological processes where various intracellular and extracellular pathways are activated and coordinated in order to restore tissue integrity. Through such physiological processes the body replaces damaged cells and restores function to the injured tissues. These processes occur in various overlapping phases including vascular response, inflammatory response, proliferation and maturation.

Skin wound healing is achieved through the interaction between epithelial and dermal cells, and the extracellular matrix, which are coordinated by a number of stimuli. The endogenous bioelectrical current represents an essential stimulus involved in wound healing. In normal conditions, the human skin exhibits bioelectrical potentials, where the external surface is more electronegative compared to the internal environment of the body. However, an injury to the skin causes an alteration of these bioelectrical potentials. This is because an injury provokes ions to leak out through the wound, which becomes more negative compared to the distal, intact tissue, where the epithelial integrity and ion transport properties remain unaffected.

Natural endogenous voltage gradients not only predict and correlate with growth and development but also drive wound healing and the regenerative processes. Changes in bioelectrical activity are observed after wounding of many tissues, especially epithelia, and are necessary for the normal healing process. These changes in bioelectrical activity in the wounded tissue that are present during the healing process appear to regulate the response.

In fact, augmenting or inhibiting such bioelectric activity results in improved or reduced wound healing respectively. Moreover, the magnitude of the endogenous electric current within the wound correlates well with the rate of wound healing. Indeed, it has been shown that blocking the passage of bioelectrical currents can slow or abolish the healing response in a variety of tissue types.

Numerous other studies have provided further evidence that bioelectric potentials are dynamic in nature, and are associated with wound healing both in animals and plants. These phenomena play an essential role in providing the signalling that coordinates the regenerative process. For example, highly regenerating animals, such as salamanders, can regenerate hearts, limbs, lower jaws, and brain tissue, and there is evidence to suggest that bioelectrical potentials are a key factor.

In a human study conducted by Wolcott and et al., MCS was applied to treat patients with ulcers of varying aetiology. The majority of these patients had failed to respond to other conservative treatments. The patients received MCS application for an average of eight weeks. The results showed that, following MCS application, the wound volume mean decreased by 82%, with an average healing rate of 13.4% per week. 34 lesions (40%) healed completely. The study provides evidence that MCS promotes healing of a variety of skin ulcers.

In accordance with these findings, a number of other studies showed that MCS promotes the healing of several types of ulcers, such as those due to diabetes,

pressure ulcers following spinal cord injury, and ulcers resulting from venous and arterial insufficiency. MCS was applied as an adjunct to conventional treatment, and ulcers healed more quickly and completely, compared with those receiving conventional treatment alone.

Moreover, another study showed that MCS treatment is more effective in promoting skin graft healing following thermal injury than conventional treatment. Various case studies demonstrate that MCS administration is beneficial in accelerating healing and reducing bacteria load in infected venous ulcers, recalcitrant pilonidal sinus and pressure sores.

The skin is the largest organ of the body, located at the interface between external and internal environment, requiring the presence of efficient sensory capabilities in order to provide the central nervous system with important information. Nociceptors are also present within the skin, which are activated by factors such as wounding and inflammation, which then cause pain. MCS promotes wound healing and reduces inflammation, thereby contributing to alleviating pain. This is because nociceptive pain normally resolves when the tissue damage heals and inflammation subsides.

Recognition of the role that bioelectricity plays in wound healing, tissue repair and pain management provides a rationale for the therapeutic administration of MCS, especially in cases where the natural repair mechanism is impaired by disease.

Conclusion

In conclusion, traumatised and dysfunctional tissue is characterised by an alteration in the endogenous bioelectrical potentials. The affected area exhibits a higher electrical resistance, decreased electrical conductance and reduced cellular capacitance compared with the surrounding tissue, thereby hindering the flow of endogenous bioelectrical current. The affected cells also exhibit a reduction in ATP synthesis, a disruption of the sodium-potassium pump, and decreased membrane transport. This is associated with impairment of the healing process and development of inflammation and pain.

Furthermore, a reduction in blood supply caused by muscular spasms, leads to local hypoxia and accumulation of noxious metabolites, thereby accentuating the healing impairment and exacerbating pain.

The physiological mechanisms responsible for the therapeutic effects of MCS can be explained by the ability of this technique to stimulate cellular physiology, repair and growth. MCS application to an injured or dysfunctional site augments the current flow, allowing cells in the affected area to regain their normal capacitance. Resistance is reduced, permitting bioelectricity to flow through and re-establish homeostasis.

Moreover, MCS application increases ATP and protein synthesis, augments substance transport across the membrane and blood flow, and improves inflammation and infection. All these factors help to initiate and perpetuate the many biochemical reactions and sustain the physiological processes that are essential for promoting healing and improving pain. Thus, MCS offers physicians an effective and versatile treatment, as the application of this technique allows a significant improvement in rapid pain control, and acceleration of healing and promotion of tissue health.

At NuroKor, we design and engineer multimodal, evidence-based electrotherapy technology that incorporates a number of formulations, including MCS.

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