ELECTROMEDICINE: THE WAVE OF THE FUTURE

Ava Frick, DVM
Animal Fitness Center, PC, Owner/Director
Veterinary Medical Director, Electromedical Products International, Inc.

We can appreciate entering a dark room, flipping a switch, and having electrical energy generate light. Edison took care of that one for us back in 1879. We can even enjoy photos electronically generated and sent all over the world in seconds via the internet. I'm not saying that every one of us understands exactly how all that happens, but we appreciate the fact that it can be done and utilize the service.

As doctors we have looked at ECGs, EMGs, EEGs; all graphs of electrical energy patterns or waves in the body registered and printed. Taking it a step further are CT Scans, MRIs, brain mapping; image impressions generating a greater perspective of the internal energy pictures happening within the body. And now we can take those electrical images, perceived and recorded by an electrically generated device and send them electronically to anywhere in the world.

With this acceptance and use of external electrical energy, we now need to focus on the function of electromedicine in augmenting the healing process within a body. Research in the field of electromedicine has boomed within the past thirty years. Dr. Robert O. Becker was one of the premier physicians and authors studying energy medicine in the past century. In 2004 he wrote: "We are now in the process of revising the past century's biochemical concept, under which all major life processes are chemical in nature, to one that proposes that such processes are electromagnetic in nature. Because the practice of medicine is a direct descendant of each new scientific paradigm we now have 'energy medicine' as an alternative to 'chemical medicine.' This new paradigm rests quite solidly on the fact that all chemical reactions are basically electrical or electromagnetic in nature."[(1)]

While the premise of utilizing microamperage current to reduce pain, treat anxiety, depression, insomnia, and heal wounds may not be consistent with what we were originally taught, scientists and yes, doctors, can no longer refute the evidence brought forth.

This presentation is in three segments. Case presentations will be included during the lecture and at the end of each segment.

ELECTROMEDICINE: BACTERIA AND WOUNDS

Electricity travels the road of least resistance.

Electricity was first used to treat surface wounds over 300 years ago when charged gold leaf was found to prevent smallpox scars.[(2)] Experimental animal wound models demonstrated that electrical intervention resulted in accelerated healing with skin wounds resurfacing faster, and with stronger scar tissue formation.[(3,4)]

Moist wounds resurface up to 40% faster than air-exposed wounds.[(5)] When a wound is dry, its bioelectric current flow is reduced. The moisture may allow endogenously produced

current to flow more readily through the injury, and thus promote wound healing. Externally applied electrical stimulation of the wound may have a similar effect, and also tends to increase the amount of growth factor receptors which increases the amount of collagen formation.[6]

Wounds initially contaminated with Pseudomonas and/or Proteus were usually sterile after several days of microcurrent electrical therapy, MET.[7] Other investigators have also noticed similar improvements and encourage the use of this therapy as the preferred treatment for indolent ulcers.[8,9,10] Additionally, no significant adverse effects resulting from electrotherapy on wounds have been documented.[11] A review of the literature shows that MET is an effective and safe supplement to the non-surgical management of recalcitrant leg ulcers.[12]

Robert O. Becker, MD demonstrated that electrical current is the trigger that stimulates healing, growth, and regeneration in all living organisms.[13] He found that repair of injury occurs in response to signals that come from an electrical control system, and suggested that this system became less efficient with age.

Becker developed his theory of biological control systems based on concepts derived from physics, electronics, and biology. He postulated that the first living organisms must have been capable of self-repair otherwise they never would have survived. The repair process requires a closed-loop system. A specific signal is generated, called the current of injury (COI), which causes another signal to start repair. The COI signal gradually decreases over time with the repair process, until it finally stops when the repair is complete.

All our senses (e.g., smell, taste, hearing, sight and touch) are based on a pulse or vibrational signal system. The body controls the activity of cells responding to the senses by producing specific direct current electrical environments in their vicinity. It also appears to be the primary primitive system in the brain, controlling the actions of the neurons in their generation and receipt of nerve impulses. Given this understanding, the application of the correct form of electrical intervention is a powerful tool for initiating the endogenous mechanisms for healing.

Chang proposed another mechanism for MET. His research showed that microcurrent stimulation increased adenosine triphosphate (ATP) generation by almost 500%. Increasing the level of current to milliampere levels actually decreased the results. Microcurrent was also shown to enhance amino acid transport and protein synthesis in the treated area 30 to 40% above controls.[14]

Adenosine triphosphate is an essential factor in the healing process. Large amounts of ATP, the cell's main energy source, are required to control primary functions such as the movement of vital minerals, like sodium, potassium, magnesium and calcium, into and out of the cell. It also sustains the movement of waste products out of the cell. Injured tissues are deficient in ATP. As MET restores circulation and replenishes ATP, nutrients can again flow into injured cells and waste products can flow out. This is necessary for the development of healthy tissues.

It would be helpful to review the cellular nature of an injury to fully appreciate the importance of Chang’s research. Trauma will affect the electrical potential of cells in damaged

tissues.[14] Initially the injured site has a much higher resistance than that of the surrounding tissue. Basic physics dictates that electricity tends to flow towards the path of least resistance. Therefore endogenous bioelectricity avoids areas of high resistance and takes the easiest path, generally around the injury. The decreased electrical flow through the injured area decreases the cellular capacitance.[15] As a result, healing is actually impaired. This may be one of the reasons for inflammatory reactions. Pain, heat, swelling, and redness are the characteristics of inflamed tissues. Electricity flows more readily through these hot inflammatory fluids.

The correct microcurrent application to an injured site augments the endogenous current flow. This allows the traumatized area to regain its capacitance. The resistance of the injured tissue is then reduced allowing bioelectricity to enter the area to reestablish homeostasis. Therefore microcurrent electrical therapy can be viewed as a catalyst helpful in initiating and sustaining the numerous chemical and electrical reactions that occur in the healing process.[16, 17]

ELECTROMEDICINE: PAIN

Pain is invisible – its symptoms are not.

Pain is now considered the fifth vital sign and multimodal pain management has a large focus in most veterinary practices today. Pain is complex and must be viewed in light of a complexity-based model in order to fully appreciate disease, illness, and individuality. Giordano laid it out when he said, “Pain can be considered to be a spectral disorder – one that ranges from a symptom of organic insult or trauma, to durable, more global pathologic changes occurring at multiple levels of the nervous system, ultimately affecting the substrates that are involved in and/or elicit behavior, emotion, and cognition of the (internal and external) environment and, thus, some form of the definable ‘self’.”[18]

We need to consider not just the duration of pain (acute vs. chronic) but the full impact of its presence on and in a body. The terms nociceptive and neuropathic have been adopted in the human medical field of pain management to further delineate and more adequately define the etiology and pathophysiological processes known as pain.

Eudynia has been proposed to represent physiological ‘normal’ or nociceptive pain and maldynia to be ‘abnormal’ pain arising from neuropathic processes. That concept alone does not wholly impute the significance of abnormality. Maldynia taken further produces, and results from, functional and structurally maladaptive changes in the nervous system that evokes, and is reciprocally affected by, alterations in cognition, emotion, and behavior.

If we as veterinarians truly want to treat the dynamic of pain, we need to focus on more than the appearance of pain itself toward a neurophilosophy of pain. The mere functional and structural changes in the neurological axis that maldynia encompasses extends from periphery to brain. It is the global impact of the specific brain regions that are involved, which induce upon self where the greatest individual effect may lie. Maldynia can evoke a sense of alterations in the being’s consciousness of its internal state. Knowing this elevates our responsibility to treat pain centrally, as well as peripherally, and to utilize as many available resources as possible.[18]

Preemptive pain management is important to reduce the likelihood of central nervous system sensitization. Reducing maldynia (a duration extending past 3-6 months) involves reversing physiological alterations within neural pathways that led to hypersensitivity and antinociceptive input resistance, the result of the generation of repeated pain signals.

The International Association for the Study of Pain lists over 200 clinical chronic pain syndromes. Among them priorities for veterinarians include osteoarthritis, degenerative disc disease, cancer, and phantom limb pain.[19] The importance of the volume of potential chronic pain sources is that it is more prevalent than what we may realize and the impact on the animal's life quality is huge. Some of the potential adverse effects of pain include:[20] Impaired immune function, cardiopulmonary stress and dysfunction, sympathetic dominant system with chronic adrenal activation, increased metabolic rate, inflammatory mediator and cytokine production, peripheral and central nervous system hyperalgesia, tissue damage, water retention, ileus, and increased blood clotting and lysis.

Many mechanisms, chemical mediators, mineral and protein alterations, neurotrophic factors, and other yet undetermined interactions can lead to the establishment of chronic pain pathways. Tissue damage causes the production and accumulation of ions, peptides, lipids and proteins such as growth factors and cytokines in the injured tissue; all of these are known to sensitize nociceptors.

Vanilloid-receptor 1 (VR-1) is a protein that converts heat into a receptor potential and is sensitized by chemical mediators found at inflammatory sites. Hydrogen ions, lipids, and protons can activate VR-1 inducing a sustained excitation of nociceptors. Neurotrophic factors generated during injury modulate sensory transduction mechanisms. Nerve growth factor (NGF) elicits changes in sensory neurons via long-term changes in gene expression and act within minutes to sensitize isolated neurons.[21]

Glutamate, magnesium ions, and calcium are necessary at receptors in the dorsal horn in preventing the emergence of central hypersensitization and transition from acute to chronic pain. All of the chemical and nutritional stimuli mechanisms and yes, even vibrational and electrical stimulation, activate nociceptors based on the understanding of conventional ligand-receptor-binding wisdom discovered by Candace Pert, PhD.[22]

The pain pathway is a maze of nerve fibers (country roads, streets, highways, and interstates interconnected by clover-leafs and cross-roads) traveled by an untold number of messengers (cars, trucks, semis, motorcycles, bicycles, joggers) driven by chemicals and reactors (women, men, young, old, scientists, home-makers, farmers, teachers, students) fueled by a variety or sources (fuel both for the vehicle and for the individual in the form of gas, diesel, nutrition, electrical energy, etc.). While no single drug or even a combination thereof acting synergistically could be expected to ameliorate pain at every location or source, the objective of blocking the four physiological processes of transduction, transmission, modulation and perception[23] can be interceded with the application of microcurrent electrical therapy (MET) and cranial electrotherapy stimulation (CES) without the sides effects of drugs.

Transduction – introduce inhibition at peripheral sensitization of nociceptors
Transmission – introduce inhibition of impulse conduction

Modulation – modulate the spinal pathways and introduce inhibition of central sensitization
Perception – inhibit or alter the body's perception and response to pain centrally

I previously discussed mechanisms of MET in healing but it is also widely used in treating both eudynic and maldynic pain associated with cancer pain,[24] back pain, [25] spinal pain, [26] and orthopedic rehabilitation pain.[27]

MET uses current in the microamperage range, 1000 times less than that of TENS and below sensation threshold. This is significant when treating cutaneous sensitive species such as horses and cats and the young. The pulse width, or length of time that the current is delivered per unit of time, is much longer with microcurrent devices than with other electromedical technologies. A typical pulse is about 0.5 seconds, which is 2,500 times longer than the pulse in a typical TENS unit and a good MET device has approximately ten times the electronic circuitry of a TENS unit.[28]

The results seen in pain management applications seem to fall into mechanisms other than those accounted for by the 1965 Gate Theory proposed by Melzack and Wall.[29] Research has reported chemical and physiological changes following microcurrent studies in many animal species.[30] The overall effect involves systemic mechanisms minimally encompassing the peripheral lesion, pituitary gland, thalamus, limbic system, and the cerebral cortex.

Phantom limb pain is a real problem in people and we could expect it as well in animals though they don't express it as such. Ronald Melzack first looked at the central pain mechanisms and theorized the existence of anatomical locations within the cortex. When chronic pain existed or body loss occurred associated with pain, that area on the cortex became larger, a greater focal point, than it naturally deserved.[31] Following an amputation where afferent input from a site is lost, the body will attempt to reconnect to other neuromodules in an effort to make up for lost stimulation. These new connections often result in referred pain.[32]

Electromedicine, specifically combining peripheral microcurrent and cranial electrotherapy stimulation, is a highly effective treatment protocol for both acute and chronic pain patients.[33,34,35,36,37] CES is an approach to effectively alter pain pathophysiology in the brain. A study performed on primates where receptor electrodes were placed across varying sites in the brain, showed that CES current across the head sent electrical impulses through every area of the brain focusing heavily in the limbic system.[38] "That means that CES stimulates the brain's pain neuromatrix directly and it also stimulates the limbic, or emotion center of the brain, either one or both of which could be important in altering or raising the threshold of the pain message."[37]

In my clinical practice the past six years I have overseen the administration of thousands of CES and MET treatments for associated pain conditions in dogs, horses, cats, rabbits, guinea pigs, hamsters, rats, alpacas, and cows. While the etiologies varied; arthritis, DJD, post-operative pain, cancer pain, injuries, spinal pain and dysfunction (both cervical and thoracolumbar), abdominal pain, phantom limb, radiculopathies and other referred pain syndromes, the bottom line was the same. The animal hurt. A single treatment takes from 20 to 60 minutes depending on the specific condition and severity of pain. Many treatments are

performed in-clinic followed by leasing a medical device to the clients where they continue the therapy at home.

Revisiting the four physiological processes of pain; transduction, transmission, modulation and perception; electromedicine can positively affect patient outcome at each of those levels when used as part of a multimodal pain management protocol.

ELECTROMEDICINE: BEHAVIOR

Mental states are the only thing in life that truly matter to animals.

Behavior is the result of a mental state. Mental states are derived from feelings, which are comprised of life's enjoyments and pleasures as well as life's discomforts, fears, miseries, and sufferings. Mental states are the only thing in life that truly matter to animals.[40] It is a reflection of quality of life and as veterinarians we should be asking ourselves, "Are we treating this patient in a manner that is adding quality to its life?" For animals can only measure the moment. There is no projection into the future and time is not a consideration.

Behavior is also a reflection of the state of the Autonomic Nervous System (ANS). Animals can be out of tune with their ANS and the end result will be seen as a change in behavior. For a dog in a sympathetic dominant state it might be separation anxiety, gastrointestinal malfunction, fear biting, becoming afraid of thunderstorms, unexplained aggression, or obsessive compulsive issues. A sympathetic dominant horse may exhibit stall walking, cribbing, wall-banging, escape maneuvers, or biting. They can also develop digestive disorders and gastric ulcers in association with a sympathetic overload or sympathetic/parasympathetic mismatch. Cats can develop obsessive compulsive disorders, aggression, chronic digestive problems, and psychoses. When the parasympathetic system is dominant the animal may be lethargic in nature, slow moving, obese in stature and generally a couch potato.

The state of emotions are separated into primary or basic emotions and secondary or complex emotions. The six primary emotions include the innate and reflexive such as joy, surprise, fear, grief, anger, and disgust. These are linked to the Sympathetic system and are housed in the limbic system, which is similar in many different mammals and crosses species lines. Each has a unique facial expression with associated body posture and vocal tones. These are recognizable across cultural boundaries and species lines.

Secondary emotions are combinations of primary emotions superimposed on appetites or drive states and are exhibited as social emotions such as love, guilt, shame, and embarrassment. These are believed to be shared by species other than humans because they are associated with social bonds necessary for all mammalian survival. Emotional neglect can impair social, emotional, and behavioral development in animals, oftentimes permanently.

Emotions evoke action, somatic and visceral motor activity, and aversive behavior in the face of fear and disgust. Social interaction and attachment activate the neuropeptides oxytocin and vasopressin. These emotions are therefore dependent on a functioning hypothalamic-pituitary axis.[41, 42,43]

The neuroanatomical primary control mechanisms for eating and aggression are located in the hypothalamus. They are however modulated by cortical limbic structures through thalamic pathways.[44] Without a balanced functioning Autonomic Nervous System the possible altering effects on an individual's response to environmental and emotional situations is as varied as the number of animals in existence.

For example, genotypic variation can produce phenotypic distinctions in the structure and function of diverse systems (e.g., enzymes, ion channels, signaling and structural proteins) that can affect physiological processes ranging from metabolism to cognition. The addition of a pain factor can induce epigenetic effects within the central nervous system. Individual variances further acknowledge the importance of appreciating from a broader perspective the encompassing nature and reflectivity of body, brain, mind, behavior, and environment as part of a complex hierarchical system acting within a particular individual.[45]

Many researchers and clinicians have a theory that disregulation of the brain's firing patterns is responsible for most of the behavioral anomalies. The thalamus is seen as the command center directing information traffic to and from the body, to the cortex, and back again. Its firing pattern determines whether alpha, beta, theta or delta waves will be predominant in a part of the brain at any given time and in what combinations
These patterns then determine much of one's behavior.

Normal thalamic function can be altered by a variety of psychological and physical trauma resulting in deranged firing orders from the thalamus. Deranged firing orders from the thalamus to other areas of the brain can result in depression, anxiety, insomnia, ADD, eating disorder, addictions, and OCD. Their conclusion is that most health problems arise from overarousal, underarousal, or instability in the CNS.[46]" "…The proposed net effect of multiple streams of diverse information reaching into and being sent back to the cerebellum is that the cerebellum integrates multiple internal representations with external stimuli and self-generated responses. The cerebellar contribution to these different subsystems permits the ultimate production of harmonious sensorimotor, cognitive, and affective autonomic behaviors."[47]

Cranial Electrotherapy Stimulation (CES) is a prescription medical device that when applied can benefit many patients experiencing emotional upsets and an unbalanced ANS, imparting positive physiological and behavioral changes.[48,49] The noninvasive application of low levels of microcurrent (less than 1 to 3 microampere in animals) applied across the head can normalize the overall firing pattern of the thalamus and bring it back into homeostasis. Clips are applied to the ears utilizing the eighth cranial nerve as access to the brain. CES was named in 1978 by the FDA's Neurology Panel after new laws required the assessment of the safety and effectiveness of prescription only devices then on the market.[50,51]

A double-blind study done by Clark, Mills, and Marchant in England in 2000 evaluated the potential efficacy of Alpha-Stim® CES in horses for stress reduction. Thirty three behavioral traits including body locomotion, head motion, ear position, oral behavior, and lower lip response were monitored. All of the changes were highly intercorrelated and strongly indicated a reduction in the horses' state of arousal following CES treatment that was not noted in the sham treatments.[52]

Alpha-Stim® CES can change the electrical and chemical activity of certain nerve cells in the brainstem thereby amplifying activity in some neurological systems, and diminishing the activity of others, such as in the hypothalamus. This form of CES engages distinct populations of "on" and "off" modulatory cells of the serotonergic (5-HT) raphe nuclei of the brainstem reticular formation. 5-HT inhibits brainstem cholinergic (ACh) and noradrenergic (NE) systems that project supratentorially. This suppresses thalamo-cortical activity, arousal, and agitation, alters sensory processing and induces an EEG alpha rhythm. As well, 5-HT can act directly to modulate pain sensation in the dorsal horn of the spinal cord, and alter pain perception, and cognition and emotionality within the limbic forebrain.(53)

Electromedicine in the form of CES can produce within the body an electrical activity pattern known as an alpha state, as measured by EEGs.(54) The resultant central and peripheral effects of feelings of calmness, relaxation, increased mental focus, decreased stress-effects, reduced agitation, stabilized moods and the ability to control both sensations and perceptions of particular types of pain, makes cranial electrotherapy stimulation a welcome modality in treating patients with behavior disorders.(55)

ELECTROMEDICINE: THE WAVE OF THE FUTURE - CLOSING

Our future is a reflection of our willingness to experience now what we may not wholly believe.

The only thing constant in life is change. There is much we have yet to learn but the experience of it requires permission; permission from oneself to reach beyond belief and make a change. Veterinarians should be willing to make a change of ones mindset in order to better serve our moral, ethical, and obligatory role as animal caretakers. Electromedicine has become a part of scientific history and is the wave of the future. It offers a safe, effective mode of treating a variety of conditions and can be used alone or in conjunction with current traditional therapeutic protocols.

> *"Studies in animals have clearly established that various forms of electrical stimulation positively affect the growth, repair, and remodeling of hard and soft tissue. The level of interest in animal studies of electrical stimulation is rising rapidly, and new understanding, in parallel with studies in vitro and in the clinic, will continue to be gained. The future holds the promise of a wide range of conditions being routinely treated by electrical stimulation, based in part on progress in studies in animals."* (Black J: Electrical Stimulation of hard and soft tissues in animal models. *PubMed* – PMID: 388661)

References available from the author.

References

1. “Exploring New Horizons in Electromedicine”, *The Journal of Alternative and Complementary Medicine.* Vol. 10, No. 1, 2004, pp17-18.
2. Robinson KR. Digby's receipts. *Annals Med History.* 1925;7:216-19.
3. Carey LC, Lepley D. Effect of continuous direct electric current on healing wounds. *Surgical Forum.* 1962;13:33-35.
4. Assimacopoulos D. Low intensity negative electric current in treatment of ulcers of leg due to chronic venous insufficiency: preliminary report of three cases. *American Journal of Surgery.* 1968;115:683-687.
5. Eaglstein WH, Mertz PM. New method for assessing epidermal wound healing: the effects of triamcinolone acetonide and polyethylene film occlusion. *Journal of Investigative Dermatology.* 1978;71:382-384.
6. Falanga V. Electrical stimulation increases the expression of fibroblast receptors for transforming growth factor-beta. *Journal of Investigative Dermatology.* 1987;88:488.
7. Spadara JA, Berger TJ, Barranco SD, et al. Antibacterial Effects of Silver Electrodes with Weak Direct Current. *Amtimicrobial Agents and Chemotherapy,* Nov 1974, p.637-642.
8. Barron JJ, Jacobson WE. Treatment of decubitus ulcers: a new approach. *Minnesota Medicine.* 1985;68:103-105.
9. Lundeberg TC, Eriksson SV, Malm, M. Electrical nerve stimulation improves healing of diabetic ulcers. *Annals of Plastic Surgery.* 1992;29(4):328-31.
10. Alvarez OM. The healing of superficial skin wounds is stimulated by external electrical current. *Journal of Investigative Dermatology.* 1983;81:144-48.
11. Weiss DS. Electrical stimulation and wound healing. *Archives of Dermatology.* 1990;126:222-225.
12. Dayton PD, Palladino SJ. Electrical stimulation of cutaneous ulcerations: a literature review. *Journal of the American Podiatric Medical Association.* 1989;79:318-321.
13. Becker RO. *The Body Electric*. New York:William Morrow and Co., 1985.
14. Chang N, Van Hoff H, Bockx E, et al. The effect of electric currents on ATP generation, protein synthesis, and membrane transport in rat skin. *Clinical Orthopedics.* 1982;171:264-72.
15. Windsor RE, Lester JP, Herring SA. Electrical stimulation in clinical practice. *Physician and Sportsmedicine.* 1993;21:85-93.
16. Frick AL, McCauley D Microcurrent electrical therapy heals a recalcitrant wound in a horse, *Journal of Equine Veterinary Science* 25(11): 418-22, 2005.
17. Frick AL, *Veterinary Wound Management Society,* www.VWMS.com, Nov 2006.
18. Giordano J. Commentary: Dolor, Morus, Patiens: Maldynia, Pain as Illness and Suffering. *The Pain Practioner,* Vol. 16, No 1, 9-11.
19. IASP Task Force on Taxonomy. Pain terms: A current list with definitions and notes on usage. In: Merkey H, Bogduk N, editors. *Classification of Chronic Pain.* 2nd ed. Seattle (WA): IASP Prerss; 1994. p209-14.
20. Lamont LA, Tranquilli WJ, Grimm KA. Philosophy of pain. *Vet Clin North Am Small Anim Pract* 2000;30(4):703-28.
21. Millis DL, Fox SM. Chronic Pain: Origin and Management. *Novartis* 2004.
22. Pert C. *Molecules of Emotion The Science Behind Mind-Body Medicine,* Simon & Schuster, New York, NY 1997.
23. Tranquilli WJ, Grimm KA, Lamont LA: Pain Management for the Small Animal Practitioner. Jackson (WY): Teton NewMedia; p1-11, 2000.

24. Bauer W. Electrical Treatment of Severe Head and Neck Cancer Pain: *Arch Otolaryngol.* Vol 109, June 1983.
25. Kirsch DL, Smith RB. The use of cranial electrotherapy stimulation in the management of chronic pain: A review, *NeuroRehabilitation* 14(2000)85-94.
26. Tan G, Rintala D, Herrington R, et al: Treating spinal cord injury pain with cranial electrotherapy stimulation (abstract). *Journal of Spinal Cord Medicine.* 26(3) 2003.
27. Sizer P, Sawyer S, Brismee J, et al. Postoperative Pain After Patellar Tendon-bone Anterior Cruciate Ligament Reconstruction. Presented at the *American Physical Therapy Association* Annual Conference, Indianapolis, IN; June 2000.
28. Mercola JM, Kirsch DL. The basis for microcurrent electrical therapy (MET) in conventional medical practice. *Journal of Advancement in Medicine.* 1995;8(2):107-120.
29. Melzack R, Wall PD. Pain mechanisms: A new theory. *Science* 1965;150(699):971-9.
30. Kirsch DL. *The Science Behind Cranial Electrotherapy Stimulation* 2nd ed., Medical Scope Publishing Co., Canada 2002 p103-117.
31. Butler DS. *The Sensitive Nervous System*. Noigroup Publications, Australia 2000.
32. Melzack R: Phantom Limbs. *Scientific American.* 1992; 266:120-126.
33. Kirsch DL, Smith RB: The use of cranial electrotherapy stimulation in the management of chronic pain: A review. *NeuroRehabilitation* 14(2000) 85-94.
34. Kirsch DL: Electromedical Treatment of Headaches. *Practical Pain Management,* Nov/Dec 2006.
35. Hefferman M: The Effect of Variable Microcurrents on EEG Spectrum and Pain Control. *Canadian Journal of Clinical Medicine.* Vol 4, No 10, Nov 1997.
36. Lee T-K, Lee K-S, Jeun S-S, Hong Y-K, et al. The control of chronic pain using microcurrent electrical therapy and cranial electrotherapy stimulation. From the Department of Neurosurgery, Kangnam St. Mary's Hospital, College of Medicine, and the Catholic University of Korea, Seoul, Korea. Presented at the Korea Society for Stereotactic & Functional Neurosurgery, April 14, 2004.
37. Kirsch, DL: Cranial Electrotherapy Stimulation in the Treatment of Fibromyalgia. *Practical pain Management,* Sept 2006.
38. Kirsch DL. *The Science Behind Cranial Electrotherapy Stimulation* 2nd ed.,Medical Scope Publishing Co., Canada 2002 p109.
39. Kirsch DL, Lerner FN. Electromedicine: The Other Side of Physiology, *Pain Management, A Practical Guide for Clinicians, Ch 55.* CRC Press, Boca Raton, FL 2002.
40. McMillan, Franklin D: A world of hurts – is pain special? *JAVMA 2003;* 223 (2).
41. Moskovitz PA. A Theory of Suffering. *The Pain Practitioner* 2006; 16 (1):74-81.
42. Bekoff M. Minding Animals. New York: *Oxford University Press,* 2002.
43. Panskepp J. Affective Neuroscience. New York: *Oxford University Press,* 1998.
44. Houpt KA, Wolski TR: Domestic Animal Behavior for Veterinarians and Animal Scientists. *The Iowa State University Press,* 1992; 54-57, 72-73.
45. Giordano J. Good as Gold? The Randomized Controlled Trial: Paradigmatic Revision and Responsibility in Pain Research. *The Pain Practitioner* 2006; 16 (2):66-69.
46. Robbins, J. A symphony in the brain, *Grove Press* 2000; 200-202.
47. Schmahmann. The Cerebellum and Cognition, *Int Rev Neurobiology*, Vol. 41.
48. Shealy CN, Cady RK, Culver-Vehoff D, Cox R, Liss S. Cerebral spinal fluid and plasma neurochemical: response to cranial electrical stimulation. *Journal of Neurological and Orthopaedic Medicine and Surgery* 1998:18(2):94-07.

49. Childs, A. Cranial electrotherapy stimulation reduces aggression in violent retarded population: a preliminary report. *The Journal of Neuropsychiatry and Clinical Neurosciences,* 17(4): 548-551, 2005.
50. Kirsch DL, Smith R. Cranial electrotherapy stimulation for anxiety, depression, insomnia, cognitive dysfunction, and pain. *Bioelectromagnetic Medicine* Paul Rosch, ed.; 2004, 727-740.
51. Gilula MF, Barach PR. Cranial electrotherapy stimulation: a safe neuromedical treatment for anxiety, depression or insomnia. *Southern Medical Journal.* 97(12): 1269-1270, 2004.
52. Clark N, Mills D, Marchant J. Evaluation of the potential efficacy of the Alpha-Stim SCS in the horse. DeMontfort University Equestrian Centre and Field Station, Caythorpe, Lincolnshire, United Kingdom. January 2000. (Available online at: http://www.alpha-stim.com/Information/Technology/Research/Research_PDF/horse_study.pdf)
53. Giordano J. *Putative Mechanisms of Cranial Electrotherapy Stimulation (CES): Effects and Implications* and *How Alpha-Stim® Cranial Electrotherapy Simulation (CES) Works,* www.alpha-stim.com
54. Hefferman MS. Comparative Effects of Microcurrent Stimulation on EEG Spectrum and Correlation Dimension. *Integrative Physiological and Behavioral Science* 1996 31 (3);202-209.
55. Kirsch DL. *The Science Behind Cranial Electrotherapy Stimulation* 2nd ed., Medical Scope Publishing Co., Canada 2002.