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ACVP

Test-driving CARs to Treat Canine Lymphoma

According to Nicola J. Mason, PhD, BVetMed, DACVIM, associate professor of medicine and pathobiology at the University of Pennsylvania School of Veterinary Medicine in Philadelphia, adoptive cell transfer (ACT) is an emerging form of cellular therapy that in its current form involves collecting, manipulating, and reinfusing the patient's own immune cells back into the body to treat cancer. Ex vivo manipulation of these cellular products frequently includes activation and expansion of either T cells or natural killer (NK) cells and genetic modification to redirect their antigentic specificity against

Nicola M. Parry, BVSc, MRCVS, MSc, DACVP, ELS

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FEATURE

Electroceuticals: The Wave of the Future Is Now

Increasingly, treatment for a host of conditions and ailments is based on electroceuticals rather than pharmaceuticals. Instead of prescriptions for chemical molecules, some doctors are prescribing specific frequencies, waveforms, and amplitudes for their patients. This is not science fiction–it's happening right now.

It's not really a stretch to see how this can be. Every day, car engines are started and doors are opened from a distance using a fob. This is made

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MVC

Advances in Feline Heart Disease Diagnosis

Cats are more adept than dogs at hiding clinical signs of heart disease, according to Rebecca Stepien, DVM, DACVIM, clinical professor of cardiology at the University of Wisconsin School of Veterinary Medicine. That's why it is important to use multiple available diagnostic tools to detect and stage cardiac disease in cats.

Natalie Stilwell, DVM, MS, PhD

At the 2018 Midwest Veterinary Conference in Columbus, Ohio, Dr. Stepien presented the latest tools for diagnosis of cardiac abnormalities in cats. She began by emphasizing the importance of differentiating heart disease and heart failure in the feline patient.

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UROLOGY

Canine Urinary Incontinence

Urinary incontinence (UI), a common problem encountered in small animal practice, can result from congenital anatomic abnormalities, urine retention and overflow incontinence, or sphincter incompetence. The timing of the onset of UI and the ability of a dog to empty its bladder are important in determining the underlying cause. Behavioral changes are important factors as well.

This review focuses on 2 of the most common causes of UI: urethral sphincter mechanism incompetence (USMI) and functional urethral obstruction

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EQUINE MEDICINE

US Study Examines Equine Parasite Control Practices

Until recently, parasite control in equids commonly relied on treatments at frequent, fixed intervals and little to no diagnostic surveillance of parasite burden. Due to the widespread occurrence of cyathostomin and ascarid resistance to anthelmintic treatment, the American Association of Equine Practitioners

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PARASITOLOGY

Developing a Vaccine for Lyme Disease

Lyme disease is the most commonly reported vector-borne disease in humans in the United States.[1] Its incidence in dogs has been increasing steadily due to expanding tick populations.[2] In a webinar hosted by online continuing education provider VETgirl (vetgirlontherun.com), Richard T. Marconi, PhD, talked about

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MVC

Antibiotic Selection in Pyoderma

Bacterial pyoderma is one of the most commonly diagnosed dermatologic diseases in dogs. Although β-lactam antibiotics such as cephalexin were once effective in treating pyoderma, the growing emergence of resistant bacteria, particularly methicillin-resistant *Staphylococcus*, has made treatment of this condition much more complicated.

At the 2018 Midwest Veterinary Conference in Columbus, Ohio, Paul B. Bloom, DVM, DACVD, DABVP (Canine and Feline), discussed the diagnosis and treatment of pyodermas,

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Electroceuticals: The Wave of the Future Is Now

Although still in its infancy in veterinary medicine, targeting neural circuits with electricity offers huge potential to provide focused, personalized treatment for a variety of ailments.

By Ava Frick, DVM, CVC, FAIS

Microcurrent electrical therapy on the elbow of a dog with degenerative joint disease.

(*continued from front cover*)

possible by matching frequency signals (waves) that are programmed to initiate a ligand–receptor type of reaction, allowing people to enter a warm space and be on their way. Photos and messages are relayed daily by the millions from one phone to another. Images and videos (waves, frequencies) travel through space, not getting crossed with others and reaching their intended destinations intact.

WHAT ARE ELECTROCEUTICALS?

Simply, electroceuticals, which are sometimes called bioelectronics, are electric waveforms that stimulate the nervous system electronically and modify bodily functions. Waveforms, frequencies, and microamperes—collectively called microcurrent electrical therapy (MET) and cranial electrotherapy stimulation (CES)—are being used to stimulate cell regeneration and treat injuries, acute and chronic pain, anxiety, depression, and insomnia.[1-6] MET and CES work because the nervous system and tissues function electrochemically and can be modulated readily by electrical intervention. Low-frequency current effectively targets cell receptors, activating them through frequency matching in a manner similar to that of chemical ligands.

THE PIONEERS

Robert O. Becker, MD, an orthopedic surgeon known as the father of electromedicine and electrochemically induced cellular regeneration, began studying electric current therapy in 1970. Fifteen years later, he demonstrated that electric current is the trigger that stimulates healing, growth, and regeneration in all living organisms. Signals come from an electric control system that he called the current of injury, which is conducted through Schwann cells and the myelin surrounding neurons.[7]

In 1980, Candace Pert, PhD, published her research on ligand–receptor binding, providing a new understanding of cellular physiology and the connection between mind and body.[8] Bjorn Nordenstrom, MD, proposed a model of biologically closed electric circuits analogous to closed circuits in electronic technology. He postulated in 1998 that mechanical blood circulation is closely integrated anatomically and physiologically with a controlling bioelectric system.[9]

Taking the research findings of these and other pioneers, neurobiologist Daniel L. Kirsch, PhD, DAAPM, FAIS—whose mentor was Dr. Becker—patented a unique waveform. He collaborated with engineer Raymond Chan to design medical devices for implementing pain and stress control technologies into clinical systems. His Alpha-Stim technology was the first dual electromedical device (MET and CES) to be cleared by the Food and Drug Administration to market in 1981. Dr. Kirsch remains at the forefront of research in this field.[2] Today, the Alpha-Stim and Fisher Wallace Stimulator (formerly Liss Cranial Stimulator) are the primary electroceutical devices on the market.

EARLY RESEARCH

As for many drugs, early research on MET and CES was conducted using animals. Once safety was established, the focus turned to human studies and clinical trials. Because the current is subsensory, it lends itself well to double-blind placebo-controlled crossover studies.

Animal studies in neurophysiology and electromedicine continue to yield new discoveries on the efficacy of this therapeutic approach. Measurements have shown that CES current across the head sends electric impulses through every area of the brain. CES directly stimulates the brain's neuromatrix, including the limbic area, or emotion center, of the brain.[10,11]

Results of an experimental study in rats with CES documented as much as a 3-fold increase in beta-endorphins after only a single CES treatment.[12] Results of a double-blind study looking at 33 behavioral traits in horses treated with CES showed that all 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 (**Box**).[13]

Neurosurgeon C. Norman Shealy, MD, assessed beta-endorphin and serotonin levels in plasma and cerebrospinal fluid (CSF) following a 20-minute session of CES and found that beta-endorphins measured 98% higher in plasma and 219% higher in CSF. Serotonin levels were 15% to 40% higher in plasma and 50% to 200% higher in CSF.[14]

Results from further research have shown the effectiveness of CES in treating fibromyalgia, posttraumatic stress disorder, spinal cord injury, cancer pain, and dental anxiety in humans.[15-18] Results of low-resolution electromagnetic tomography and functional magnetic resonance imaging studies have shown that select waveforms can reach most cortical and subcortical areas of the brain, thereby altering the brain's emotional centers (ie, thalamus, hypothalamus, basal ganglia, reticular activating system, cerebral cortex, and limbic system) where the amygdala controls the strength of emotional responses, especially for fear and anger.[11]

HOW ELECTROCEUTICALS WORK

Cells throughout the body manufacture peptides that act as ligands to surface receptors on other remote cells, communicating via the extracellular fluid and circulatory system. Cells within a specific organ or tissue system communicate through specific frequencies in the microamperage range, activating the current of injury and causing the system to tend toward homeostasis. Neuromodulation imparts an electric signal with a frequency that perfectly matches the receptors in the body to resonate and activate intracellular responses.

MET can act similarly to ligands in activating receptors to send their messages into cells and produce effects resembling a wide range of chemical messengers. MET can be viewed as a catalyst

CLINICAL STUDY NOW ENROLLING

Electromedical Products International (EPI) is sponsoring a multisite cohort study to evaluate the tolerability and efficacy of Alpha-Stim cranial electrotherapy stimulation in dogs with anxiety, aggression, or stress-related behavior. If you are a veterinarian interested in participating, please contact the EPI research division at 800-FOR-PAIN.

in initiating and sustaining the numerous chemical and electrical reactions that occur in the healing process. An effective biphasic, squared, long-pulse-width waveform in the microamperage range (1000 times less than that of a transcutaneous electrical nerve stimulation device and below sensation threshold) will use resonant frequencies to activate central pain modulatory mechanisms.

The sensation of pain is transmitted through the body along billions of nerve cells that are designed specifically to transmit messages through electrochemical signals. Physics controls chemical reactions in the body, and most bodily functions can be normalized electrically. It is the application protocol that affects the peripheral pain site directly and accesses the central nervous system by directing the current through the spine. Combining MET and CES addresses all 4 pain pathways: transduction, transmission, modulation, and perception.

The resultant central and peripheral effects of CES include calmness, relaxation, reduced agitation and aggression, stabilized mood, improved sleep, and reduced pain. Results will vary with the exact technology used, the pathology of the disease being treated, the overall health and hydration of the patient, and owner compliance. Patient history, prior medical interventions, previous injuries, and surgical scars can affect overall outcome as well.

Waveforms can be used effectively to activate the body's natural electric impulses.

USE IN ANIMALS

CES and MET have been used extensively in the clinical setting for nearly 2 decades to initiate cellular regeneration and control not only acute and chronic pain situations, such as arthritis, spinal injury, nerve conduction deficiencies, cancer, sprains, strains, wounds, and surgical pain, but also such stress-related conditions as anxiety, insomnia, cognitive dysfunction states, noise phobia, and depression. Prescription MET and CES devices are long lasting, cumulative, safe, effective, easy to use, portable, and nonaddictive, and have no known tolerance concerns. Adverse effects are minor and self-limiting, primarily consisting of skin irritation.

Treatments can be applied in clinic by the technical team, and devices can be prescribed for use at home with a short in-clinic training session. Initially, the best results will be achieved when treatments are applied twice a day, but in-clinic treatments administered 2 to 3 times per week will also be beneficial. Follow-up patient assessment includes clinical observation, range of motion, change in posture, use of extremities, calmness, improved sleep, appetite, attitude, and behavior.

CONCLUSION

As an aid to endogenous bioelectric currents, electroceuticals can accomplish miraculous things. They may in fact work better in the absence of any interference from factors based on our previous, limited, chemical-dominant view of physiology. Today and in the future, disorders of both the body and mind might be better treated using a range of frequencies that have the potential to treat a variety of pathologies effectively without the risk of harmful adverse effects. ■

References available at AmericanVeterinarian.com.

Dr. Frick is a leading authority in the application of microcurrent therapy for animals. Her focus on physiotherapy has spanned over 20 years and her research has been published in the *Journal of Equine Veterinary Science*, *Innovative Veterinary Care Journal*, and the *Journal of the American Holistic Veterinary Medical Association*.

BOX. Pilot Study: Cranial Electrotherapy Stimulation in Horses[13]

Researchers in the United Kingdom have evaluated the potential use of cranial electrotherapy stimulation (CES) in horses. In a pilot study that took place at De Montfort University Equestrian Center in Lincolnshire, anxiety-related behaviors and physiologic signs in adult horses were recorded before, during, and after 20-minute treatment sessions with the Alpha-Stim CES unit.

An initial study with 6 apparently healthy adult horses determined acceptance of the Alpha-Stim device at incrementally increasing levels. Horses displayed relaxed behavioral signs, including wobbling of the head and quivering lower lip, beginning when exposure was set at level 2.

In the main study, 8 adult horses each received 4 treatment sessions with Alpha-Stim. During the sessions, an experimenter entered the horse's stall only to adjust the exposure level on the Alpha-Stim, then left to record detailed behaviors related to locomotion as well as head, ear, and lip movements. A heart rate monitor was also placed to record changes in heart rate during the sessions. Each Alpha-Stim session included four 10-minute phases, with the device set as follows:

- Phase 1: Level 0
- Phase 2: Level 2
- Phase 3: Level 2 (including a "sham approach" by the experimenter pretending to adjust the device)
- Phase 4: Level 0

Although a high level of individual variation in heart rate existed, the investigators found that the mean heart rate in 7 of 8 horses significantly decreased within 10 to 20 minutes of Alpha-Stim treatment at exposure level 2 (**see chart below**). The decrease in heart rate was most pronounced for those horses with the highest baseline heart rates.

Additionally, the proportional amount of time spent displaying relaxed versus tense behaviors changed with Alpha-Stim treatment sessions. In particular, horses displayed relaxed behaviors, such as dozing and head wobbling, more frequently during and/or after Alpha-Stim treatment than before treatment. By contrast, other behaviors commonly associated with tension and frustration, such as alert body posture, a tense lower lip, ear flicking, and head shaking, were displayed less frequently by the majority of horses after 10 to 20 minutes of Alpha-Stim treatment. In many cases, the relaxed behaviors persisted when Alpha-Stim exposure was turned back to level 0, suggesting that the device offers persisting anxiolytic effects.

Thus, the authors proposed that Alpha-Stim has potential use for the treatment of anxiety-related issues in horses.

Mean Heart Rate for Study Horses Across the 4 Trial Phases