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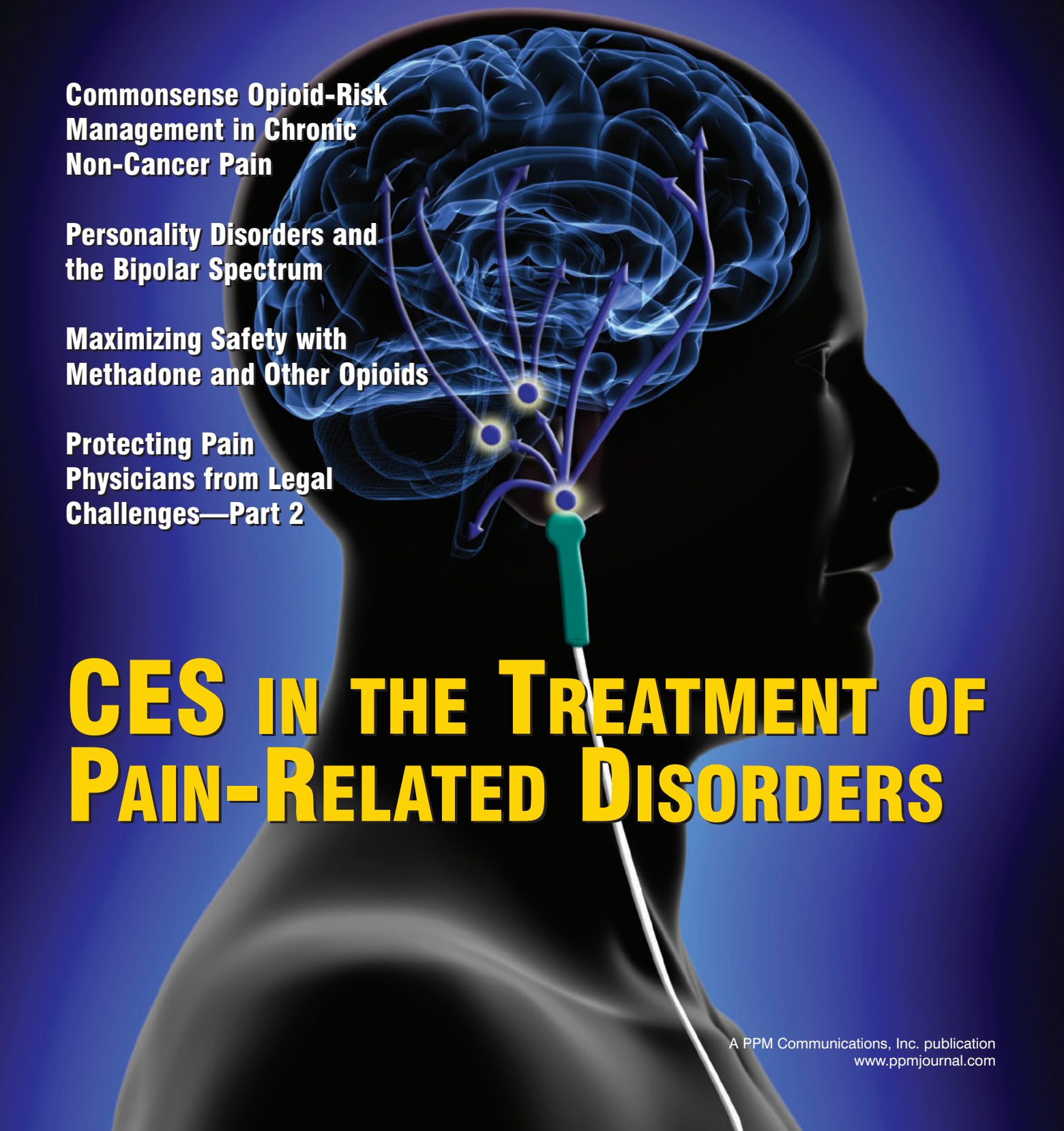

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CES IN THE TREATMENT OF PAIN-RELATED DISORDERS

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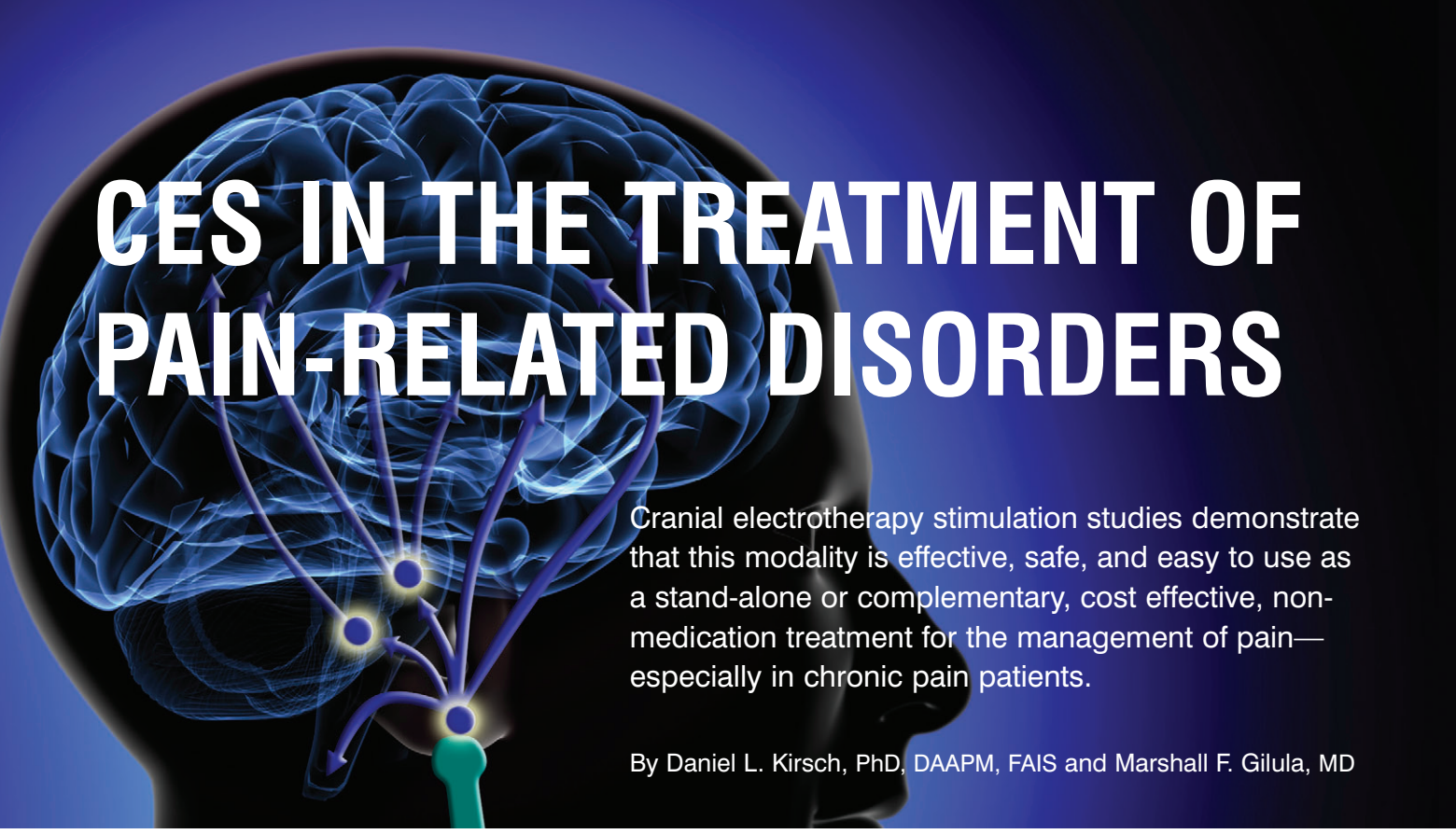

CES IN THE TREATMENT OF PAIN-RELATED DISORDERS

Cranial electrotherapy stimulation studies demonstrate that this modality is effective, safe, and easy to use as a stand-alone or complementary, cost effective, non-medication treatment for the management of pain—especially in chronic pain patients.

By Daniel L. Kirsch, PhD, DAAPM, FAIS and Marshall F. Gilula, MD

Cranial electrotherapy stimulation (CES) is now being used and studied as a treatment for centrally-mediated pain syndromes that have historically been refractory to intervention, such as fibromyalgia, multiple sclerosis, spinal cord injuries, and global reflex sympathetic dystrophy. The safety assured by the low level of current and positive effects seen on the electroencephalogram also make CES a potentially efficacious treatment for headaches and dental pain. This review of the available data on CES suggests that sufficient research findings are now available to establish the usefulness of CES in pain management as a stand-alone or add-on treatment. This paper presents supporting data for a sequence of different ways that CES has been evaluated in pain management. These include rigorous double-blind crossover studies, open clinical trials, physician surveys, patient self-report surveys, reductions in anesthetic requirements, and dental applications for a variety of challenging pain-related disorders.

Background

Cranial electrotherapy stimulation (CES) involves the application of small amounts of current, usually less than one milliampere (1,000 microamperes), through the head via ear clip electrodes, for the purpose of treating a variety of psychological and medical disorders. CES came to the United States in the late 1960s under the somewhat misleading name, electrosleep. It had been developed in the Soviet Union in the 1950s and quickly spread throughout the former Eastern Bloc, then into Europe, Asia, and much of the West. It was already in use in Japan when it finally arrived in the US in the 1960s. By the late 1960s, it was being researched in both animal and human subjects at several U.S. medical schools, including the University of Texas at San Antonio,[1] the University of Wisconsin[2] and the University of Tennessee.[3] Major research reviews in 1985,[4] 1995,[5] 2002,[6] and most recently in 2006-2007,[7-17] summarized the progress of CES in American medicine. The US Food and Drug Administration now certifies CES devices that have met its standards to be sold by prescription for the treatment of anxiety, insomnia, and depression. CES has been approved for sale without a prescription in all of Europe, Canada, Mexico, Australia, Scandinavia, parts of Asia, South America, Latvia, Turkey, the Middle East, and Africa.[18]

The treatment of pain is the most rapidly evolving application of CES. In addition to a direct effect on various brain centers and relays, this modality may also raise the pain threshold due to the stress-reducing effects that occur when anxiety and depression are reduced. While patients exhibit significant responses to the usual research protocol of one hour treatment daily for three or four weeks, chronic pain management often requires CES to be used over longer periods of time from devices that are prescribed for home use. The progressive pathology underlying many chronic pain disorders limits CES to palliative relief. However, for long term pain management, CES has the added benefits of being anxiolytic, antidepressive, and helpful in insomnia, as well as being safe and cost-effective.

Dr. Ronald Melzack became interested in central pain mechanisms from his studies of phantom limb pain in which, for example, a left leg amputee could experience intense pain seemingly in the missing left foot.[19] Melzack theorized the importance of a pain homunculus in the cortex that represents every part of the body. Afferent fibers ascend from a given body area site to its corresponding site on the homunculus. In this theory, *neuromodules*—residing in a larger *neuromatrix* that encompass the homunculus—normally send pain messages to the forebrain when sufficiently stimulated. The sources of stimulation are afferent pain fibers ascending to the neuromatrix by way of the spinothalamic tract.

When the afferent input from a specific body site is terminated, the neuromodule

RESULTS OF A PHYSICIAN SURVEY OF 500 PATIENTS

500 total N	174 male (age range 5-87, mean 41)	21 inpatients	
	326 female (age range 9-92, mean 44)	423 outpatients	
Treatment(s) used prior to Alpha-Stim CES:			
36 ECT	122 physical therapy	46 sedative-hypnotics	
111 psychotherapy	46 surgery	6 psychostimulants	
41 behavior modification	51 other non-drug	49 major tranquilizers	
55 milliampere TENS	36 alcohol	52 analgesics	
39 chiropractic	51 anxiolitics	122 NSAIDs	
26 nerve blocks	148 anti-depressants	105 muscle relaxants	
13 biofeedback	87 narcotics	73 other drugs	
Reason(s) for discontinuing prior treatment:			
44 still using	10 exacerbated	23 negative drug effects	2 moved
140 not efficacious	12 too expensive	9 uses Alpha-Stim	38 other
Side effects of prior treatment:			
74 none	25 felt drugged	20 sedation	
10 pain	9 drug sensitivity/allergy	17 GI discomfort	
6 addiction	12 mental cloudiness	26 other	

Treatment Results Obtained by Using Alpha-Stim CES

Chief Complaints	# Reported	Worse (neg)	None (no change)	Slight (<24%)	Fair (25 - 49%)	Moderate (50 - 74%)	Marked (75 - 99%)	Complete (100%)	Significant Improvement (>25%)
Pain	286	1 0.35%	5 1.75%	20 6.99%	48 16.78%	77 26.92%	108 37.76%	27 9.44%	260 90.91%
Anxiety	349	0 0.00%	8 2.29%	14 4.01%	39 11.17%	89 25.50%	181 51.86%	18 5.16%	327 93.70%
Depression	184	0 0.00%	8 4.35%	11 5.98%	31 16.85%	38 20.65%	82 44.57%	14 7.61%	165 89.67%
Stress	259	0 0.00%	6 2.32%	12 4.63%	37 14.29%	70 27.03%	124 47.88%	10 3.86%	241 93.05%
Insomnia	135	0 0.00%	16 11.85%	12 8.89%	17 12.59%	34 25.19%	45 33.33%	11 8.15%	107 79.26%
Headache	151	1 0.66%	8 5.30%	6 3.97%	25 16.56%	32 21.19%	63 41.72%	16 10.60%	136 90.07%
Muscle Tension	259	2 0.77%	6 2.32%	6 2.32%	42 16.22%	76 29.34%	111 42.86%	16 6.18%	245 94.59%
Treatment results obtained prior to use of Alpha-Stim CES									
Prior Treatments	389	24 6.17%	95 24.42%	116 29.82%	75 19.28%	51 13.11%	28 7.20%	0 0.00%	154 39.59%

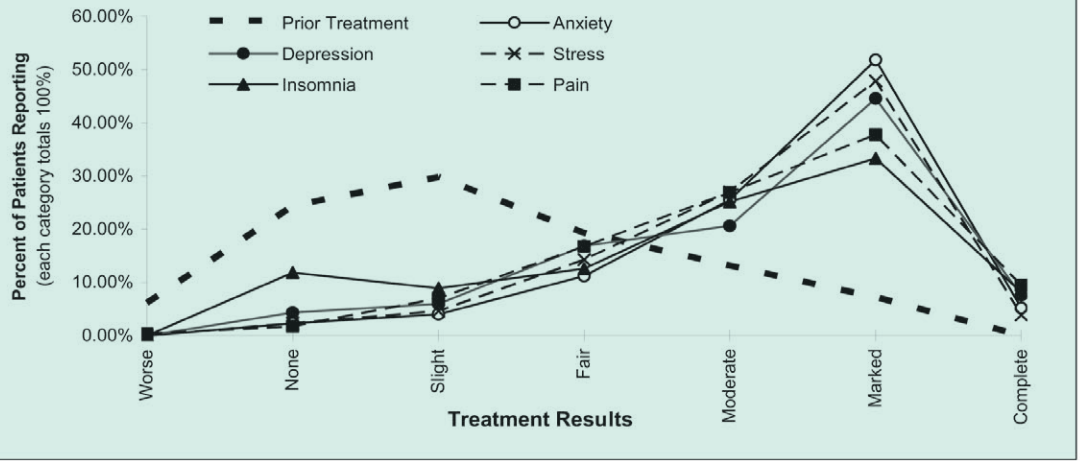

TABLE 1. *Summary of the results of CES grouped according to 7 symptoms. The results were obtained from 47 physicians who reported on multiple pain-related symptoms in 500 patients. Both the Table and its associated chart provide a comparison with the results of prior treatment.*[6]

Peer-Reviewed Outcomes on CES Patients' Self-Reports						
Condition	**N**	**Slight <24%**	**Fair 25-49%**	**Moderate 50-74%**	**Marked 75-100%**	**Significant >25%**
Pain (all cases)	1949	136 6.98%	623 31.97%	74 138.02%	449 23.04%	1813 93.02%
Back Pain	403	20 4.96%	109 27.05%	157 38.96%	117 29.03%	383 95.04%
Cervical Pain	265	18 6.79%	69 26.04%	125 47.17%	53 20.00%	247 93.21%
Hip/Leg/Foot Pain	160	6 3.75%	43 26.88%	53 33.13%	58 36.25%	154 96.25%
Shoulder/Arm/Hand Pain	150	13 8.67%	41 27.33%	63 42.00%	33 22.00%	137 91.33%
Carpal Tunnel	25	0 0.00%	5 20.00%	17 68.00%	3 12.00%	25 100.00%
Arthritis Pain	188	11 5.85%	51 27.13%	88 46.81%	38 20.21%	177 94.15%
TMJ Pain	158	17 10.76%	60 37.97%	60 37.97%	21 13.29%	141 89.24%
Myofascial Pain	62	6 9.68%	18 29.03%	18 29.03%	20 32.26%	56 90.32%
Reflex Sympathetic Dystrophy	55	10 18.18%	16 29.09%	19 34.55%	10 18.18%	45 81.82%
Fibromyalgia (alone)	142	13 9.15%	53 37.32%	52 36.62%	24 16.90%	129 90.85%
Fibromyalgia (with other)	363	33 9.09%	131 36.09%	152 41.87%	47 12.95%	330 90.91%
Migraine	118	2 1.69%	49 41.53%	30 25.42%	37 31.36%	116 98.31%
Headaches (all other)	112	20 17.86%	30 26.79%	24 21.43%	38 33.93%	92 82.14%

TABLE 2. *Results of using CES at least three weeks from consecutive patient surveys.*[26]

involved extends dendrites to other neuromodules in an apparent attempt to make up for the new lack of stimulation. Referred pain can result from such new cortical connections.[20]

It has long been known that stress can decrease the pain threshold.[21] This applies especially to stressful situations in which the person senses or experiences a lack of personal control.[22] Emotional disturbance such as anger or fear can be a real source of stress, as can unwanted noises or lack of sleep.

CES is a way to effectively alter pain pathophysiology in the brain. Given the myriad of cortical processes that may contribute to the experience of pain, it stands to reason that a form of electrical stimulation with proven efficacy in other centrally mediated disorders such as anxiety,[5,13,14] insomnia,[8] and depression,[11,12] would also make a valuable contribution to pain management. Early CES studies—one on primates and one on a human seizure subject—in which receptor electrodes were placed at different sites in the brain, showed that CES current applied across the head sent electrical impulses throughout the brain, concentrating especially along the limbic system.[23,24] More recently, using LORETA brain imaging to determine specific cortical effects of CES, Kennerly confirmed that the current affected the entire brain.[25] Accordingly, CES stimulates the brain's entire neuromatrix directly, as well as the thalamus—an important site for pain modulation.

Surveys

Table 1 summarizes the results of a survey of 47 physicians reporting on a total of 500 patients. This gives a fair overview of the effects of CES on seven symptoms, consistent with the prospective studies.[6] This form of data is also useful to see the range of responses and average effect size that one may reasonably expect from treatment. Note that the results across the seven symptoms evaluated are fairly consistent. For example, on the low end, 0.00%-0.77% of patients became worse and 1.75%-11.85% had no change. On the high end 33.33%-51.86% had a marked improvement, and 3.86%-10.60% had a complete recovery.

To further validate the results of the physician data, another survey collated patient self-reports of their own CES treatment. Table 2 summarizes a peer-reviewed analysis of 2,500 consecutive survey forms submitted by patients who were prescribed an Alpha-Stim CES device.[26] Most had multiple diagnoses. The only inclusion criterion was that the patients had received at least three weeks of CES treatments. Pain was listed as the primary diagnosis in 1,949, or 78% of the total group. Of those patients, 93% claimed significant pain reduction of

greater than 25%, ranging from a low of 82% in chronic regional pain syndrome (reflex sympathetic dystrophy) to a high of 98% in those suffering from migraine headaches, and 100% in carpal tunnel syndrome. A majority (72%) of the patients were female. The ages ranged from 15 to 92 years with a mean of 50 years. The length of CES treatment ranged from the three-week minimum cutoff period to five years in two cases. The average period of use was 14.68 weeks, or just over 3 1/2 months. Unlike the physician survey, the patients were not asked what settings they used, how often they used it, or for what length of time. The results reported by these patients were similar to the physician survey of 500 patients, with the patients self-reports giving slightly higher ratings overall. None of the patients reported any significant adverse effects even though the survey specifically asked.

CES in the Treatment of Specific Pain Related Disorders

Fibromyalgia

Two well-conducted CES studies on fibromyalgia have been published.[27,28] These studies used a similar research protocol measuring pain levels at tender points according to the diagnostic criteria established by the American College of Rheumatology,[29] as well as self-rating scales for overall pain, sleep, feeling of well being, and quality of life. They were also given the Profile of Mood States (POMS) psychological test to assess anxiety, depression, fatigue, and cognitive function—as well as providing a Total Mood Disturbance score.

In double-blind CES protocols such as those used in the fibromyalgia studies, CES current was limited to a subsensory level of 100 microamperes so the sham treatment would appear identical in the untreated subjects who received no current at all. None of these studies found any differences from the placebo effect in the sham treated or control groups. Following the double-blind phase of the studies, the control subjects were provided a device to treat themselves with CES at home and pre- and post-treatment scores of the control subjects were also analyzed.

Lichtbroun Study. Lichtbroun found that CES yielded about a 28% reduction in tender point pain scores ($t=2.27$, $p<0.01$).[27] This is about the average reduction in pain scores found in multiple medication studies.[30] The self-rated overall pain level improved by more than 27% ($t=3.04$, $p<0.002$). Of the 60% of the patients who went into the study complaining of very poor sleep, that number dropped to 5% following the study ($t=2.05$, $p<0.02$). Fibromyalgia patients treated with CES for three weeks also experienced significant improvements in vigor ($t=2.97$, $p<0.01$, two-tailed), and fatigue ($t=1.93$, $p<0.03$, one-tailed, $p<0.06$ two-tailed; $df=38$) from psychological measurements. Significant improvements were also found in feelings of well-being ($t=1.67$, $p<0.05$) and quality of life ($t=1.92$, $p<0.03$). There was no positive placebo effect among the sham-treated patients in the Lichtbroun study.

A second arm of this study allowed patients who were in the sham group to treat themselves at home following the double-blind part of the study. The 23 of the 40 controls who agreed to be crossed over were allowed to increase the CES current. This produced even greater improvements as measured by the tender point scores ($t=3.27$, $p<0.001$), overall pain level ($t=1.68$, $p<0.05$), quality of sleep ($t=3.89$, $p<0.001$), feelings of well being ($t=5.33$, $p<0.001$), and quality of life ($t=5.23$, $p<0.001$).

Cork Study. Cork conducted the other double-blind crossover study that examined the effect of CES on pain associated with fibromyalgia.[28] He randomly allocated 39 subjects to a CES treatment group and 35 subjects to a sham treatment group. Pain Intensity, McGill Pain Score, tenderpoint score, Profile of Mood States, and Oswestry Score Measurements were taken at baseline and after three weeks. Three weeks after crossover of the sham group to active CES treatment, all measurements were repeated. Cork's study showed an improvement in pain intensity at the $p<0.01$ level compared to sham and $p<0.001$ in the sham group scores after crossover to active treatment. The McGill Score was not significant in the initial three week trial but showed a $p<0.001$ in sham group after crossover. Tenderpoint score initially showed a $p<0.01$ compared to the sham group and a $p<0.001$ in the sham group after crossover. Profile of Mood States showed a difference of $p<0.01$ compare to the sham group and $p<0.001$ in the sham group after crossover. No significant effect was observed in the Oswestry Score which is a disability scale rather than a functional assessment of pain. That prompted the authors to conclude that longer follow-up studies would be necessary to observe changes in the self-rated disability scale. The authors also concluded that CES appears to be an effective, well-tolerated treatment for fibromyalgia and those involved in the treatment of fibromyalgia should include it in their clinical armamentarium given the demonstrated safety of this non-invasive modality.

The Licthbroun and Cork studies of CES for fibromyalgia are rigorous double-blinded clinical trials. As an initial reviewer of Licthboun's study stated, "This article is certainly intriguing. The results are so positive in such a difficult-to-treat population that one becomes skeptical. Nonetheless, positive results in a double-blind controlled study need to be taken seriously."[31]

It should certainly be taken seriously now that it has been replicated by Cork in an equally rigorous university-based randomly controlled trial. While longitudinal studies still need to be conducted, the best long term data to date is from the results supplied by patients on their surveys that clearly demonstrate favorable data representing as much as two years of treatment with CES in some individuals.

As can be seen from the survey data in Table 2, 91% of patients reporting fibromyalgia and at least one comorbid symptom rated their symptoms as having improved significantly by 25% or greater. Nine percent had experienced less than 25% improvement, 36% rated their improvement as being between 25 to 49%, and the largest group of 41% rated their improvement as being between 50 and 74%. There was also a group representing 13% of the fibromyalgia patients who rated themselves as nearly symptom-free. This yields a mean effect size of $r=.65$, which means that the average fibromyalgia patients improved 65%, a very high effect size in this refractory condition.

Multiple Sclerosis

From the survey summarized in Table 2, 12 of the responses had been sent in by patients who had been prescribed a CES device for their multiple sclerosis (MS). They claimed an average improvement of 46.57% (range of 0-99%) in their symptoms. 10 of the 12 patients were female. Their ages ranged from 21-52 (average age was 39), and they had used CES for

one to eight weeks, with an average of 4.4 weeks, or one month. Based on this encouraging preliminary evidence, a small pilot study was conducted.[32] After giving informed consent, 5 patients (3 females) underwent CES treatments for one hour a day for one month, at 0.5 Hz frequency setting and at a comfortable level of current between 100 and 300 μA (microamperes). Ages ranged from 53-68 years old (average age was 60). Time since MS diagnoses ranged from 10-38 years (average of 21). Improvement was noted in 7 of the 10 symptoms measured as seen in Figure 1. Self rated spasticity improved 54%, vision improved 50%, sensory ability (ability to feel, as in the sense of touch) improved 45%, fatigue improved 40%, pain improved 29%, and hand function improved 22% in the left hand and 12% in the right hand. Bladder, cognitive, and mobility/gait function were not rated as significantly improved by these patients. The author concluded that while this is only a pilot study, the results were consistent with survey data and testimonial letters received so this pilot study is probably a fairly accurate assessment of what a physician might expect when prescribing a CES device for use by MS patients.

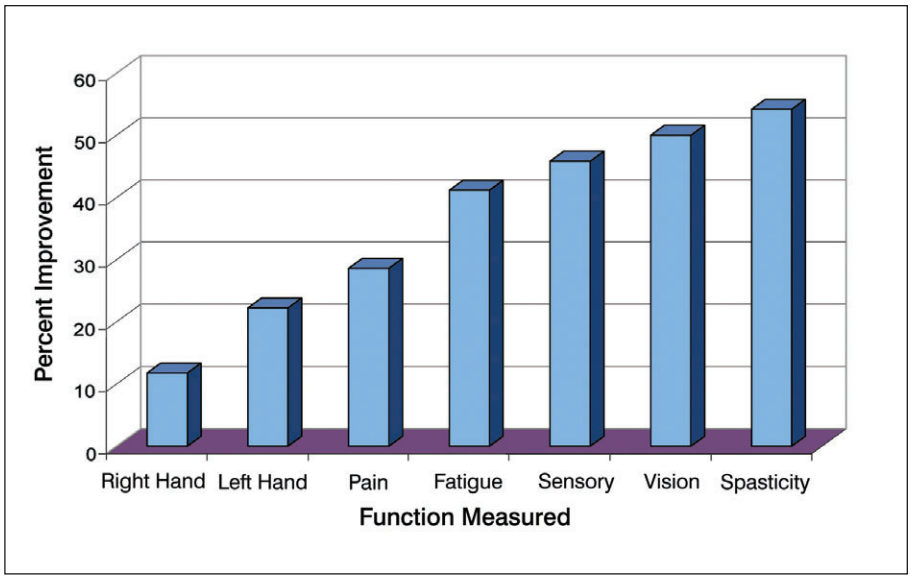

FIGURE 1. *Improvements in 5 patients diagnosed with multiple sclerosis after one month of daily CES treatments.*[32]

Spinal Cord Injuries

Spinal cord injuries (SCI) is another area that is attracting CES researchers. Wharton presented the first paper on CES for SCI at the annual meeting of the American Spinal Injury Association in New York in 1982.[33] He had completed a double-blind study of the use of CES with paraplegics and quadriplegics who were in an inpatient rehabilitation program in Dallas, Texas. Patients were given either subsensation level CES or sham CES one hour daily for three weeks, Monday through Friday. They were pre- and post-tested on standardized psychological measures of depression, anxiety, and cognitive function. It was found that patients receiving actual stimulation had significant improvement in all areas measured, while no placebo effect was found from sham treatment. The presenters reported that CES was subsequently employed routinely as a hospital treatment protocol. They reported that their physical therapists commented on patients having much better morale during muscle exercise training when they used a CES device during the mandatory passive exercise sessions. The MS patients completed their exercise sessions with little or no complaining, crying, or other emotional acting out of negativity.

A double-blind crossover study of CES for chronic pain in SCI patients was conducted in the United Kingdom.[34] Treatments were applied twice daily for 53 minutes on four consecutive days. After a washout period of eight weeks, all subjects returned to treatment and were crossed over to the opposite condition (active to sham, and sham to active). Pain decreased 51% in the treated group, but did not decrease significantly in the sham treated subjects. After crossover, the original sham subjects reported only 59% of the pain they reported at the commencement of treatment. No significant differences were determined in mood. However, analgesic and combined antidepressant and anxiolytic drug use in subjects receiving CES after crossover decreased to 46% and 53%, respectively, of the average pre-study drug use. No similar decrease in the use of the drugs was noted in the same subjects after sham treatment in the first arm of the study.

Pain levels were significantly lower ($p=0.0016$) in the CES-treated subjects as compared to sham-treated subjects ($p=0.50$). After crossover, sham subjects also showed significant improvement due to receiving the active treatment ($p<0.005$). Subjects receiving CES reported using significantly ($p<0.05$) less analgesic medication (46% of the average pretreatment level) and significantly ($p<0.05$) less (53%) of the average pre-treatment level of combined antidepressant and anxiolytic medications. No significant differences were found between groups in plasma assays. However, there were marked differences ($p<0.05$) between groups in salivary cortisol concentrations in the first arm and salivary cortisol was also lowered significantly ($p<0.05$) in the sham group after crossover to active CES treatment. Decreases in cortisol levels suggest improvements or lessening severity in the ability to handle stress.

The authors added that no adverse reactions were reported and that subjects reported a feeling of relaxation that coincided with lower blood pressure.

Another double-blind, sham controlled study with random assignment examined the effects of daily one-hour active ($N=18$) or sham ($N=20$) CES treatments for 21 consecutive days on pain intensity and interference activities.[35] Subjects consisted of 38 male veterans—six months to 60 years post SCI—receiving care at a Department of Veterans Affairs SCI Center. Treatments were self-administered at home. The active CES group reported significantly decreased daily pain intensity ($p=0.03$) compared with the sham CES group. The active CES group also showed significantly decreased pain interference ($p=0.004$).

The active and sham CES groups did not differ significantly with regard to their average pre-session pain ratings. There was a mean pain rating score of 6.46 for

the active CES group versus 6.08 for the sham CES group. The average change in daily pain intensity from pre- to post-session was significantly larger (p=0.03) for the active CES group (mean=-0.73) than the sham CES group (mean=-0.08). The treatment effect size was medium to large (Cohen d=0.76). Participants who received sham CES did not show significantly reduced pain (p=0.34), whereas participants who received active CES did show significantly reduced pain (p=0.02). After the double-blind phase, the sham group were offered the opportunity to cross over to an open label phase with an active CES device for another 21 consecutive days. The 17 sham CES participants who subsequently participated in the open label phase reported significant post-session pain reduction (p=0.003). None of the changes in the BPI pain intensity subscale items were statistically significant for any of the three groups. However, in paired t-tests for the active CES group, 7 of the 10 individual pain interference subscale items significantly changed and reflected small to moderate effect sizes. This included: general activity (Cohen d=0.67), self-care (Cohen d=0.58), sleep (Cohen d=0.53), social activities (Cohen d=0.51), normal work (Cohen d=0.45), enjoyment of life (Cohen d=0.42), and recreational activities (Cohen d=0.38). A paired t-test within the active CES group showed that the composite pain interference score for both groups decreased significantly (mean change=14.6, P=0.004, Cohen d=0.50). Neither the individual BPI pain interference subscale items nor the composite pain interference score changed significantly in the sham group (mean change=-4.7, P=0.24). After crossover into the open label phase, pain interference with sleep decreased significantly (Cohen d=0.40). Changes were greater in the three participants in the active group who had non-traumatic SCI.

The authors concluded that CES can effectively treat chronic pain in persons with SCI and may lower the burden of long-term pharmacologic management. As a result they are now conducting a large three-year multi-site study of CES for SCI in veterans.

CES is offered routinely in the pain treatment program at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas, where the above cited SCI study was conduced. A case was recently published from there of a 60-year-old Afro-American male with worsening pain from a back injury coupled with PTSD that developed while serving in Vietnam.[15] The initial treatment goals were to reduce pain, stabilize and improve sleep, and help him regain a sense of control over his daily activities. The 10-session treatment plan consisted of CES to reduce anxiety and improve sleep and was coupled with self-monitoring skills along with hypnosis to help modulate his pain and to begin the resolution of his trauma. By the seventh session, the patient was "very pleased" with treatment, his pain was mostly gone, sleep improved, and no pain medication had been taken during the previous week. At the final session he was able to get "very relaxed" using CES and hypnosis, had not been taking any pain medication, his sleep was quite regular and satisfactory and his pain had been under control and "milder." In addition to the patient's self-reported improvement in his pain and related symptoms, the BPI and the Center for Epidemiological Scale-Depression (CPS-D) indicated a number of improvements including significant reductions in pain intensity, pain interference, and depressive symptoms. The patient reported meaningful reductions of pain interference in all aspects of his daily functioning. Perhaps equally significant was a substantial reduction in pain medication use and the ability to function with minimal assistance from healthcare providers.

"The authors concluded that CES can effectively treat chronic pain in persons with SCI and may lower the burden of long-term pharmacologic management. As a result they are now conducting a large three-year multi-site study of CES for SCI in veterans."

The authors concluded that when effective, CES and hypnosis can help patients have greater confidence in treatments offered by psychologists for pain management and may help make them more open to participating in other psychological interventions that have demonstrated efficacy for pain management such as cognitive-behavioral therapy (CBT). Because of their brevity, treatments such as CES, hypnosis, and CBT can also be offered as the sole approach to patients who may not have the resources or time to participate in more time-intensive treatment.

Reflex Sympathetic Dystrophy

A case report was published on a patient referred to as 'WHH,' a 60 year old male with an intracranial traumatic brain injury (TBI) and global (full body) reflex sympathetic dystrophy (RSD).[36] In spite of severe disabilities of his brain and body, WHH continued to serve his country in his position on the Executive Staff of the President's Committee on Employment of People with Disabilities. Daily 20-minute CES treatments provided satisfactory pain relief for WHH to complete his tasks and enjoy a relatively higher quality of life than he was able to have with drugs alone.

Prior to CES, WHH has been prescribed numerous medications including Prozac 20mg q.i.d., Catapres Tab 20mg q.d., Effexor 100mg in AM and 50mg at bedtime, Levo-Dromoran 1mg b.i.d., Balofen 10mg split AM and PM, Risperdal 7.5mg at bedtime, Kolopin 0.5mg one tab 3 to 4 times per day as needed, C-Dextromthrph 60mg t.i.d., and Fentanyl patches over four years. This regime did little to reduce his whole body chronic intense critical pain and burning. Nor did it relieve his difficulty sleeping. Standard milliampere transcutaneous electrical nerve stimulation (TENS) did not help. WHH claimed these treatments made him worse and was concerned about the short- and long-term side effects the drugs had on his ability to function.

Following CES treatment, WHH exhibited marked relaxation, with a reduced anxiety level and a significantly enhanced pain threshold. Based on these positive results, he was prescribed daily 20 minute CES treatments via ear clip electrodes. WHH credits the CES treatment for allowing him to return to work and for improving his family and social life. Prior to CES, he claimed that "life was not worth living to the degree that suicide was an attractive option." He found this treatment provided him a moderate improvement of 50-74% relief from his pain, anxiety, depression, headaches, and

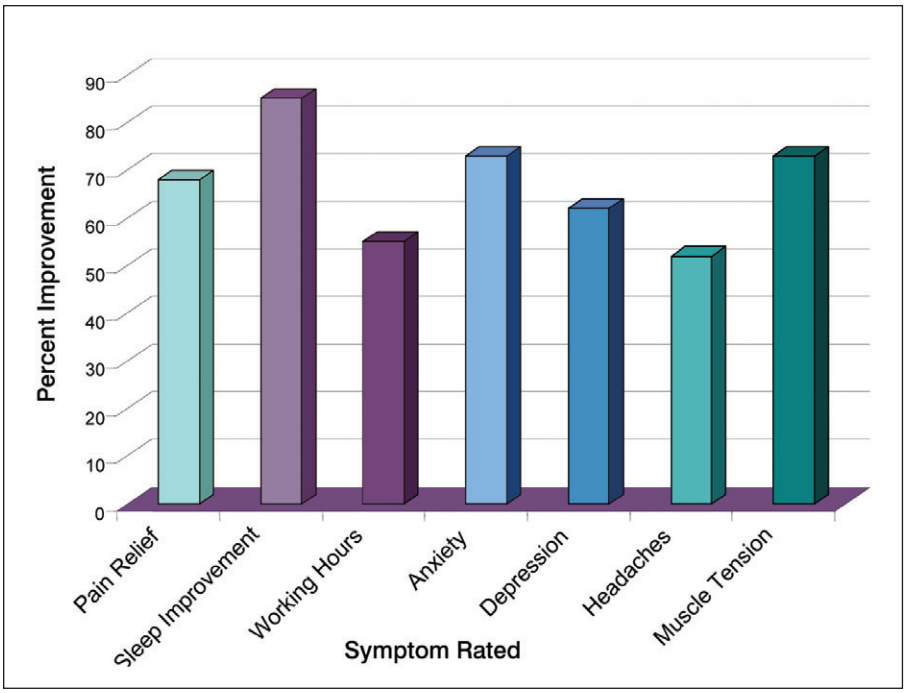

FIGURE 2. *Remarkable improvements ranging from 52% to 83% in 7 areas of the major complaints in a global RSD patient.*[36]

muscle tension, and a marked improvement of 75-99% in his insomnia, as shown in Figure 2.

The effects of a single CES treatment lasted for six to eight hours, allowing him to get through the day, then the pain gradually returned prior to the next CES treatment, but never to his pre-CES pain levels. In his own words, "The Alpha-Stim 100 has given me short term relief from my pain levels that medications have not been able to accomplish. While the relief periods may only be for eight hours or so, these near pain-free hours allow my body to recycle itself, granting me an improved quality of life. Without the Alpha-Stim 100, the constant 'level 10' debilitating pain levels leave me with no physical or emotional reserves to carry on daily life. The Alpha-Stim 100 has no side effects, whereas my medicines have profound, crippling, and lasting side effects that have impaired my bowel and colon. These impairments can not be reversed." On a zero (no pain) to 10 (maximum pain) scale, WHH says CES reduces his pain level from a 10 to a 3 which he describes as "the difference between standing on a busy street in New York at 5 PM and fly fishing on a tranquil creek." He added "CES provides me with a measure of pain relief that brings me back from the depth of despair and gives me a wedge of hope."

CES reduced his pain level to a level where he was able to perform his daily exercise routine. He was also able to rest better at night which he credits as creating a "positive emotional and physical self-environment." He reported feeling more rested in the morning. He was able to increase his work hours to 30 to 40 hours per week, up from a maximum of 15 hours prior to CES.

Following CES, his medication has been reduced to Prozac 10mg q.d., Catapres Tab 0.1mg b.i.d., Effexor 50mg AM and 25mg PM, Levo-Dromoran 1mg b.i.d., Restoril 7.5mg at bedtime, Kolopin p.r.n., and Neurontin 400mg p.r.n.

Headaches

CES reduces stress and anxiety, a commonly accepted cause for many headaches, and treats the entire head and brain. Perhaps the earliest U.S. study on headache was done as a Masters Degree thesis at the University of North Texas in Denton.[37] In that double-blind, placebo-controlled study, 18 migraine headache patients were divided into three groups of six each: a treatment group, a sham treatment group, and a placebo control group. In the treated group, CES was given for 45 minutes a day for 15 days, Monday through Friday. Over a two week period immediately following the study it was found that CES-treated patients—but not the sham-treated or placebo control patients—reported significant reductions in both headache intensity and duration.

In another study of migraine headaches—this time a doctoral dissertation research project—36 patients were assigned to biofeedback (BF) consisting of electromyogram, thermal biofeedback, and Quieting Reflex training, CES, or BF combined with CES.[38] Treatments were administered twice a week for 15 minutes each over a one month period. The patients maintained a daily record of the frequency and intensity of headaches, then followed up on the record over a one month, two month, and three month period following the initial treatments.

There was no difference between groups receiving either treatment at the end of the eight treatment sessions, but a steadily increasing cumulative improvement took place over the three month follow-up period following the study as shown in Figure 3. The BF group had an accumulative improvement of 400% while the combined BF/CES group had an accumulative improvement of 1,100% (11 times better) by the end of the third month.

Solomon studied 112 patients with tension headaches.[39] Inclusion criterion was a minimum of four headaches a week for a year, and these had to be severe enough to require treatment with prescription medications. Prior to and at the end of the study, patients rated the intensity of their headaches on a 10-point self-rating scale. The patients were asked to use CES for 20 minutes each time they had a headache and, if the pain did not go away, to use it for a second 20 minutes. The average CES treated patients' headache intensity dropped from 6.1 to 4.0 on the 10-point scale, or approximately 35% at the conclusion of the 10-week study, while the sham-treated patients reported an 18% improvement.

Romano studied the ability of CES to reduce headaches in 100 fibromyalgia patients who were asked to use CES for 4 treatment periods of 20 minute each day for up to 2 months. In this open clinical study the patients rated their improvement at 50% or greater in terms of reduced headache frequency and intensity.[40]

As shown in Table 1, 47 physicians responding to a survey treated a total of 151 headache patients with CES. They rated the treatment gain in 90% of the patients to be 25% improvement or better,

with 74% reporting at least a 50% improvement.

Patient surveys shown in Table 2 indicate that 118 patients who suffered from migraine headaches improved an average of 61%, while 112 who suffered from tension headaches improved 56%. That improvement is somewhat lower than in the migraine group, possibly due to lack of consistency in diagnostic labels or in the individual differences of neuromuscular involvement of neck or shoulder muscles that did not resolve sufficiently from CES.

Dental Pain

In a double-blind dental study, 50 patients were divided into two groups: 30 who received CES treatment and a second group of 20 receiving sham CES treatment.[41] They were randomly assigned to procedures including oral surgery, restoration, tooth extractions, root planing, pulp extirpation, and temporomandibular joint therapy.

It was found that 24 of the 30 CES patients (80%) were able to undergo dental procedures without other anesthesia, while 15 of the 20 sham-treated patients (75%) requested anesthesia. In the operative groups, 13 of 14 CES patients (93%) did not require anesthesia, while four of seven sham-treated patients (43%) did. All patients required anesthesia for endodontic procedures. All CES patients stated that the use of CES would be their first choice in future dental visits.

Another dentist used CES in 600 dental procedures over a 12-month period. 76% of the patients reported a 90% or greater reduction in pain with CES and did not request additional anesthetics.[42] When the results were broken down by procedure, 83% of the patients who underwent 71 scaling and prophylactic procedures did not ask for additional anesthesia, compared with 76% of those undergoing 473 restorative procedures, and 55% of those undergoing 29 crown preparations. One additional clinically significant finding was that all patients reported feeling more relaxed than usual while in the dental chair.

Studies of Anesthetic Equivalency

There have been two studies that assessed the equivalency of CES to various types of anesthetics. In a rather straightforward study in which he compared CES with various concentrations of N2O, Stanley gave a group of 90 urological patients and 30 abdominal surgery patients either 75%, 62.5% or 50% N2O alone or he combined a similar concentration of N2O with CES.[43] After 20 minutes of treatment, patients were given a painful stimulus with a Kocher clamp clamped at the second ratchet and applied to their upper, inner thigh for one minute. Measurements of pain included patient movement, systolic blood pressure, heart rate, respiratory rate, and minute ventilation. It was found that CES increased the potency of N2O by approximately 37% at each level, being between 0.3 and 0.4 MAC in analgesic potency when combined with N2O. The authors also found that the CES group experienced more prolonged analgesia after recovery of consciousness.

In a somewhat more elaborate study, CES equivalency to the narcotic fentanyl was studied with patients undergoing surgery. Fifty patients who were to undergo urologic operations were divided into two groups to receive either CES or sham CES in addition to normal anesthetic procedures.[44] All patients had anesthesia induced with droperidol (0.20mg/kg IV), diazepam (0.2mg/kg IV), and pancuronium (0.8mg/kg IV). Anesthesia was maintained during the surgical procedure with fentanyl given in 100 microgram IV increments every three minutes as necessary to maintain the patient at the required level of anesthesia. It was found that an average of 33% less fentanyl was required in patients who simultaneously received CES treatment.

More recently, an anesthesiologist at the Rene Descartes University of Paris, France took advantage of a personal experience to determine whether CES improved the level of postoperative analgesia by potentiating anesthetic agents used during the intra- and postoperative phases.[45] Included were analgesics injected through an epidural thoracic catheter (T8-T9) positioned at the end of an esophagectomy. Another reason for a self-experimentation was to be able to evaluate the "psycholeptic" effects of CES to gain a better understanding of the problems associated with pain treatment. CES was initiated two hours before anesthetic induction without any tranquilizer or other medication. It was then continuously applied during the entire surgical procedure and an additional 48 hours postoperatively in the intensive care unit. The usual anesthetic protocol was used during surgery. During the initial 48 postoperative hours with continuous application of CES, a decrease of the epidural anesthetic dose requirement was observed for ropivacaine and sufentanil (-25% and -60%, respectively). A similar decrease in these medications was also measured on day two, when CES was terminated. This

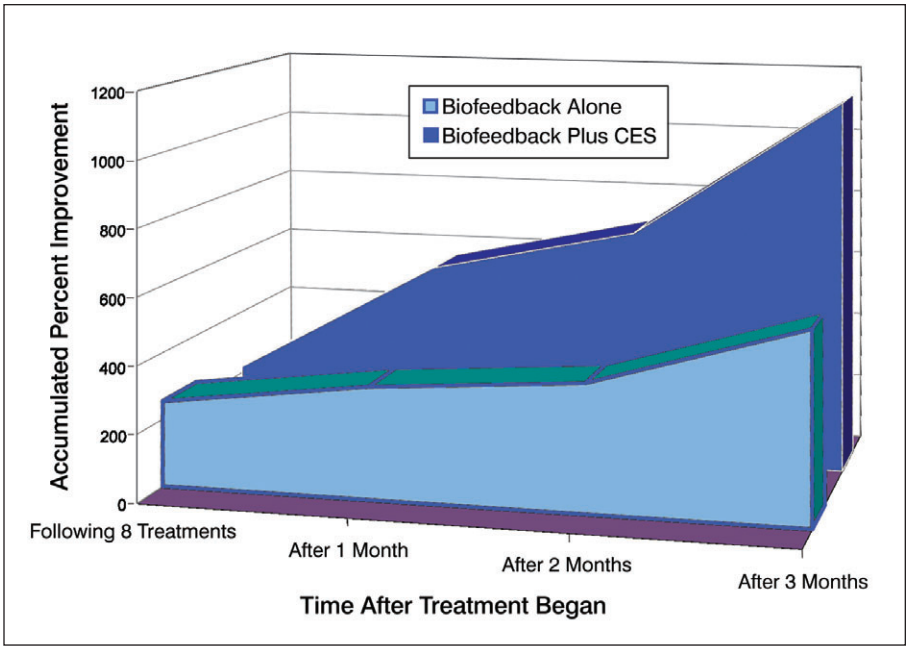

FIGURE 3. *Improvements in pain intensity and frequency ratings in migraine patients over a three month period following eight treatments of biofeedback and the addition of CES to the same biofeedback program.*[38]

decrease continued and was amplified on day three for both ropivacaine and sufentanil (-50% and -73%, respectively). On day four, the need for epidural anesthetics were totally suppressed (one day before the normal conventional weaning schedule planned for by the ICU physician with this type of surgery). The authors concluded that future clinical trials need to be conducted to show the significant advantages of CES in alternative and complementary medicine.

CES in Physical and Occupational Therapy

In a 1963 U.S. CES study, 23 patients who had been diagnosed with hemiplegia, paraplegia, and muscle spasm following traumatic injuries were given CES treatments of one hour each day for four days in an open clinical trial.[46] Muscle spasticity was tested with an electromyogram (EMG) before and just following CES treatments. A clinically significant improvement in muscle spasticity was found in all patients.

In a study of 20 children, ages 2.5 months to 15 years, with mild to severe spastic cerebral palsy, CES or sham CES was given twice a day for 10 minutes each time for six weeks in a crossover design. The results were evaluated on the Malden Gross Motor Rating Scales I, II, and III, and the Advanced Gross Motor Skills Scale. There was significant improvement in total gross motor performance in each group following the active but not the sham treatment.[47] The authors concluded that treating children who had spastic cerebral palsy with CES, combined with physical therapy, is superior to conventional physical therapy alone.

Occupational therapy (OT) alone, CES alone, or OT and CES together were provided to 16 patients diagnosed with minimal cerebral dysfunction, cerebral palsy, and spastic quadriplegia.[48] CES was given twice daily for 10 minutes over a 12 week period. Assessments were made using the Southern California Sensory Integration Test and the Jebsen hand function test. Following treatment, improvement in the design copying scores of the CES group averaged 59% compared to 35% for the OT group, and 88% for the combined treatment group. Motor accuracy improved in the CES group 43% in the dominant hand and 21% in the non-dominant hand. Improvement in the OT group was 15% in the dominant hand and 45% in the non-dominant hand. In the combined OT/CES group, improvement was 53% in the dominant hand and 68% in the non-dominant hand. In addition, the authors found that CES patients whose scores were in the moderately-impaired range during pre-testing had improved to within normal limits over the 12 weeks of CES treatment. They concluded that CES was a valuable adjunct to OT in this patient population.

"...CES may be effectively nudging the nervous system back towards a balance point that more resembles homeostasis. This may be accompanied by a reduction in stress-related hormones such as cortisol that are known to play a role in increased pain perception."

Other Pain Studies

Neurosurgeons in a Korean hospital conducted a study of 20 refractory chronic pain inpatients.[49] Daily CES treatments of one hour per day, five days a week, were given for three weeks. Ages ranged from 18 to 75 years old (mean=44 years) and 15 (75%) were female. Both CES and microcurrent electrical therapy (MET) probe treatments were given with the same device (Alpha-Stim 100) using the same waveform applied to the brain and body. Although three patients out of 20 obtained no relief from this treatment, six obtained complete relief, and eight received significant relief ranging in subjective estimation from 33% to 94%. The authors concluded that the combination of CES and MET can be an effective treatment for long-standing chronic pain, as well as for pain of shorter duration.

Discussion

The above studies represent an entire spectrum of study design ranging from case reports to survey data to open clinical trials and rigorous double-blind, placebo-controlled research. Yet in every report, treatment with cranial electrotherapy stimulation has been accompanied by some dramatic reduction in the perception of pain in every pain category studied despite the fact that most of the studies described are time-limited and have a relatively small number of subjects. One necessary caveat is that there is a huge disparity between current theories of pain and the actual knowledge of how neuroelectric devices actually work. In our current stage of knowledge, putative mechanisms of pain are quite fragmented and it becomes even more so when attempting to explain why certain modalities work as well as they do. The authors are working on a book that will detail the current state of knowledge of CES, including mechanisms.

It is not clear why putting microcurrent electrical stimulation across the head would reduce pain in the body. While some would point to a possible increase in endorphins, two studies that looked for this did not find it, although one found an increase in serotonin and a decrease in cholinesterase.[50] Another study found an increase of MAO-B in blood platelets and an increased concentration of GABA in the blood following CES treatments, but did not find an increase in serotonin, dopamine, or beta-endorphins in the blood.[51]

Animal studies suggest that CES is apparently effective in bringing neurotransmitters back into homeostatic balance when that balance is deliberately disrupted.[3] It could be possible that when the brain's normal homeostasis has been shifted into a stress pattern over a period of time—an occurrence suggested by Selye's theories to be somewhat frequent in our day and age[52]—CES may be effectively nudging the nervous system back towards a balance point that more resembles homeostasis. This may be accompanied by a reduction in stress-related hormones such as cortisol that are known to play a role in increased pain perception.

There is also increasing evidence for a central pain neuromatrix in the cortex which is responsible for processing pain messages throughout the body—according to the writings of Melzak and others. Pain messages can occur even in the absence of perceptible pathology, or in the absence of the body parts themselves—as in the examples of phantom limb pain or pain patterns persisting after the removal of organs. The neuromatrix is thought to change under certain conditions such as physical trauma of various

kinds that interrupt normal incoming stimulation. Notable researchers such as Ronald Melzack are now theorizing that the pain neuromatrix may be more important in producing chronic pain states than previously considered.[19] Accordingly, one can speculate that since CES stimulates every area of the brain this type of stimulation would include effects in the area in which the pain neuromatrix is thought to reside.[24,25,53]

From a different perspective, researchers at the St. Vincent Medical Center in Connecticut have found what appears to be occult damage in the lower medullary sensory and motor pathways in complex regional pain syndromes (reflex sympathetic dystrophy and causalgia) and fibromyalgia. They state, "We suggest that bilateral spinothalamic and corticospinal deficits, with a conspicuous ipsilateral hemisensory and hemiparetic pattern, contralateral cranial nerve XI dysfunction, and lack of other consistent cranial nerve findings are compatible with dysfunction of lower medullary sensory and motor pathways." Prior trauma was reported by 51% of their 145 patients. This group of individuals had a high incidence of whiplash injury, falls, and physical assaults.[54] It could be that CES stimulation of the medulla (using ear clip electrodes bilaterally) provides a bilaterally symmetrical stimulus into the area over time, varying only by the treatment parameters chosen.

Heffernan found that certain types of CES stimulation reduced the Fast Fourier Transform root mean square (RMS) of the EEG significantly, leveling out the peaks normally found in pain patients. The patients rated their pain as significantly reduced—coincident to the spectral smoothing of the EEG.[55] He also theorized that a significantly concentrated chaos correlation dimension in the EEG following CES suggested a heightened organization of a formerly less organized EEG in pain patients. This was accompanied by a reduction in pain and stress symptoms.[56]

The use of CES with pain patients is increasingly being supported by the outcome of a small number of well-designed research protocols as well as a large amount of pilots, careful meta-analyses, and a burgeoning amount of ethical and accurate testimonials. Its well-described efficacy in controlling some of the anxiety, depression, and insomnia ubiquitous in pain patients is a significant added benefit.

In contrast to pain medications that may carry substantial risk, side effects from CES are rare, primarily minor self-limiting problems, such as acceptability to individual patients, headaches (one in 506) and electrode burns (one in 910).[6] As a stand-alone or complementary, cost effective, non-medication treatment for the management of pain—especially in chronic pain patients—CES usage is expected to increase as practitioners become more aware of its efficacy, safety, and ease of use. CES also carries with it the clear potential for helping to increase the safety margin of nearly any medication whose dosage can be efficaciously decreased when incorporating this safe and effective neuroelectric modality into the treatment plan. ■

"CES also carries with it the clear potential for helping to increase the safety margin of nearly any medication whose dosage can be efficaciously decreased when incorporating this safe and effective neuroelectric modality into the treatment plan."

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