The use of cranial electrotherapy stimulation in the management of chronic pain: A review

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Cranial Electrotherapy Stimulation (CES) has a growing history of applications in rehabilitation medicine in the United States dating back to early 1970. As a recognized non-drug treatment of anxiety, depression and insomnia, CES gained its first major application in the field of addiction treatment and rehabilitation. By the mid 1980s research was showing additional important uses of CES in the treatment of closed head injured patients, and in paraplegic and quadriplegic patients. The most recent research is showing CES to be highly effective in the management of chronic pain patients. It may be elevating the pain threshold due to its stress reducing effects when anxiety and depression are reduced below clinical levels. Modern theorists of a pain neuromatrix in the cerebral cortex may provide an additional basis for understanding CES mechanisms in the control of pain related disorders.

1. Introduction

Cranial Electrotherapy Stimulation (CES) is the application of a small amount of current, usually less than one milliampere, through the head via ear clip electrodes. It came to the United States in the late 1960s under the rubric "electrosleep". It had been developed in the U.S.S.R. in 1954, and quickly spread throughout the former Eastern Bloc, then into Europe and most 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 US university medical schools, including the University of Texas at San Antonio, the University of Wisconsin, and the University of Tennessee [1–3]. Major research reviews in 1980 [4], and again in 1999 [5] summarized the progress of CES in American medicine.

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2. Research in rehabilitation medicine

2.1. Rehabilitation of addicted persons

The first research and subsequent use of CES in rehabilitation medicine began in the early 1970s, when research reports began coming out of the District of Columbia's 600 bed inpatient Rehabilitation Center for Alcoholics [6], and Veterans Administration Hospitals [7,8]. Following the publication of its two double-blind, placebo-controlled studies [9,10], the CompCare Corporation, then the largest rehabilitation facility in the US, if not in the world, with approximately 120 inpatient rehabilitation facilities for addiction patients, plus those with eating disorders, made the decision to put CES into their core treatment program throughout the nation. Unfortunately, there was no manufacturer of CES devices available at the time that could supply that heavy a demand for product so the plans had to be abandoned. It continued to be used in addiction treatment, however, with many facilities in both CompCare and other major addiction treatment chains making wide use of CES in their clinical treatment protocols.

2.2. The use of CES in paraplegic and quadriplegic patients

Wharton and his coworkers presented their paper "Effects of CES therapy on spinal cord injured patients" at the annual meeting of the American Spinal Injury Association in New York in 1982. They had completed a double-blind study of the use of CES with paraplegics and quadriplegics who were in an inpatient rehabilitation program in Dallas. 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 [11]. The presenters reported that CES was

subsequently employed in the hospital treatment protocol, with the physical therapists, especially, commenting that patients had much better morale during muscle exercise training when they used a CES device during the mandatory passive exercise sessions. They completed the sessions with little or no complaining, crying or other emotional negativity and acting out.

2.3. The use of CES in closed head injured patients

One of the first reports of the use of CES in closed head injured (CHI) patients appeared in 1988. It was a clinical case presentation of two CHI patients, the major focus being on their post-traumatic amnesia and subsequent cognitive deficits. It was found that following 40 minutes of CES treatment daily for three weeks, the first patient had a 55% improvement in immediate recall and a 56% increase in delayed recall. The second patient had improved 28% on immediate recall and 39% on delayed recall [12].

A subsequent double-blind, placebo-controlled study of CHI patients was published in 1994 [13]. While the major focus of the study was anxiety and depression in these patients, a side issue was the seizure disorders suffered by the patients, all of whom were on anti-seizure medication. It was not known at the time what effect CES might have on seizures. While earlier studies of addiction patients in one rehabilitation center had selectively eliminated patients known to have had withdrawal seizures, another large rehabilitation center had deliberately and successfully treated similar patients with CES to prevent withdrawal seizures [14].

During the study, one patient was observed to have a seizure and was immediately removed from further participation in the study. Following the study it was discovered that the seizure patient had been a sham-treated control and had received no stimulation. The researchers reported that when that subject's parents saw the results in the CES treated group they insisted that their son receive CES treatment. This was done, with no further seizure activity reported in this or any of the other patients who had undergone CES treatment during the study.

2.4. The use of CES in physical therapy

In an early CES study in the US, 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. Muscle spasticity was tested with an EMG device before and just following the CES treatment. A clinically significant improvement in muscle spasticity was found in all patients [15].

Another study had a serendipitous finding when researchers designed a study to see whether or not "electrosleep" actually put patients to sleep. Among 15 patients in this open clinical trial were two patients suffering from Parkinson's disease and one diagnosed with dystonia musculorum. Different types, intensities and amounts of CES current were given over several weeks of experimentation, at the end of which an unexpected finding was that the involuntary movements in the three patients with muscle dysfunction were changed in character during the passage of current, and eventually completely eliminated, as measured by EMG [16].

In another study, researchers found that in at least some types of patients, muscle tremor can be associated with the underlying level of psychological stress. While researching muscle tremor in 53 withdrawing alcoholics, researchers found that patients who were under the most psychological stress actually had fewer tremors than those who were under only moderate stress. Following 40 minutes of CES, those who formerly were under greater psychological stress began to tremor more, presumably as their stress level was reduced, while those who began under moderate levels of stress actually tremored less as their stress level fell back toward normal. Psychological stress was measured by the Minnesota Multiphasic Personality Inventory and tremor was measured with the Lafayette Instrument Steadiness Tester. It was found that benzodiazepines, 25 mg. t.i.d. and 30 mg h.s., for three to five days had no similar effect in altering the tremor of these patients, such as was found with the 40 minute CES treatment [17].

In a study of 20 children with mild to severe spastic cerebral palsy, aged 2.5 months to 15 years, CES or sham CES was given twice a day for ten 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.

The authors concluded that treating children with spastic cerebral palsy with CES in addition to physical therapy is superior to conventional treatment alone [18].

In the latest such study to appear in the CES literature, 16 patients diagnosed with minimal cerebral dysfunction, cerebral palsy and spastic quadriplegia were given either occupational therapy (OT) alone, CES

alone, or OT and CES together for 12 weeks. CES was given twice daily for 10 minutes over the 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%, for the OT group, 35%, and for the OT/CES group, 88%. Motor accuracy improved in the CES group 43% in the dominant and 21% in the non-dominant hand. Improvement in the OT group was 15% in the dominant 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 in the 12 weeks of CES treatment. They concluded that CES was a valuable adjunct to OT in this patient population [19].

3. Research in chronic pain patients

While CES treatment became much more in evidence in pain management programs in the 1990s, it was often brought in as an adjunct to pain management with the Alpha-Stim microcurrent stimulation device, which also provided CES capability. In this regard, one review noted, "(CES) is a primary modality effective for controlling anxiety, depression, insomnia and generalized stress (which is) ubiquitous in pain patients" [20].

3.1. Research in spinal pain

In 1999, a neurosurgeon used CES in an open clinical trial on spinal pain patients who were waiting in line for the implantation of dorsal column stimulators. In his study, CES was provided with Alpha-Stim SCS units applied daily for one hour a day for three weeks. The results were so impressive that he then conducted a double-blind, placebo-controlled study [21]. In the 38 patients studied, the effects of CES in reducing pain scores measured as "pain at best", "pain at worst", and "pain in general", was dramatic and significant. No positive placebo effect was found among the sham treated patients. The results of both phases of his study are combined in Fig. 1.

The researcher currently plans to replicate the study with a greater number of patients, since he feels that this is a seminal finding in the treatment of chronic spinal pain patients. A replication of this study is also just getting under way in Bombay, India [22].

3.2. Research in fibromyalgia

In 1999 a research protocol was developed for a multi-center study of the use of CES in fibromyalgia patients. The protocol provided for double-blind, placebo-controlled studies in larger medical centers and for open clinical trials in smaller treatment centers. In the double-blind protocol, the patients were to receive either CES treatment below sensation threshold at 100 microamperes of current intensity, at 0.5 Hz, on a 50% duty cycle, or sham treatment via devices set exactly like the first, but using electrodes that would not pass any current. The placebo control patients were to sit out the three weeks without access to the CES device, to serve as controls for any placebo effect in the sham-treated patients. The physician, other therapists and the psychometrician were to remain blind to the treatment conditions, as was the statistician who would evaluate the study results. Patients were to be randomly assigned to each of the research groups. All subjects were to sign patient consent forms, and each study would be run under the supervision and guidance of a local Investigational Review Board to assure compliance with local community standards in human subjects research.

Due to the strictness of the protocol, only one-third of the subjects in each study would receive actual CES treatment for their fibromyalgia. Accordingly, it was suggested that in those research centers where CES treatment was shown to be effective, any of the untreated, two-thirds of the patients who served as controls should be offered three weeks of CES treatment one hour per day, in an open clinical format, following the double-blind phase of the study. They would often receive treatment at higher current intensity since there would be no need to treat them below sensation level and they could set the intensity to any level they chose. The treatment results of those who agreed to a third testing following this treatment could be included in the report as uncontrolled, clinical data.

The first double-blind study to be completed involved 60 patients in a large private rheumatology practice in New Jersey [23]. The principle investigator had served on the national panel that developed the diagnostic protocol for fibromyalgia, and the protocol was approved by the Investigational Review Board of the Robert Wood Johnson Medical School.

Measures included the physician's evaluation of each patient's tender points pre and post study, and the patient completed ten point self rating of their overall level of pain, their quality of sleep, their feeling of well being and their quality of life. They also completed

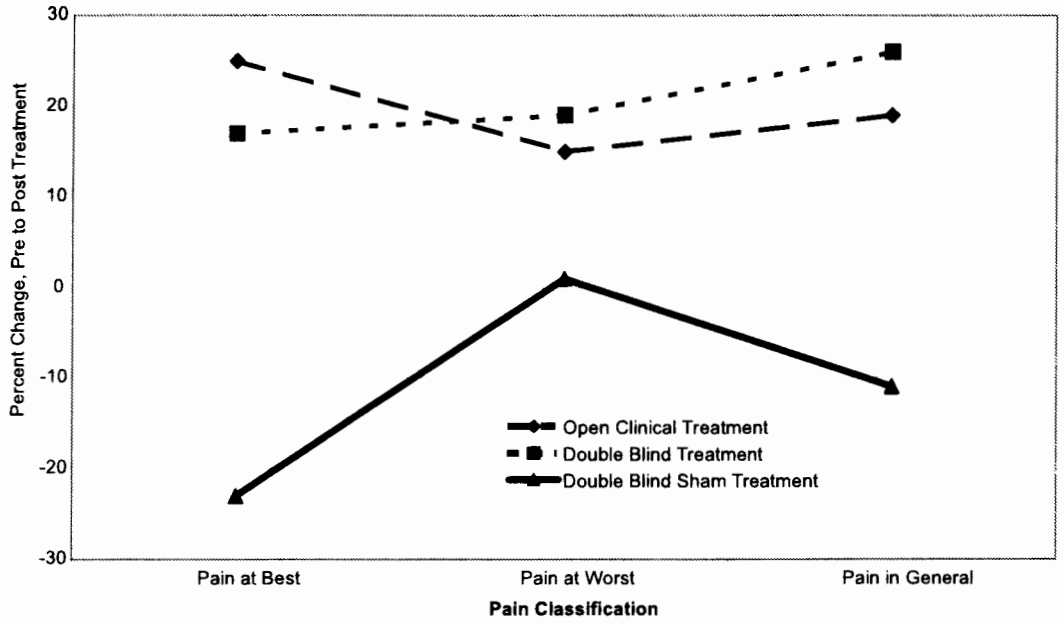

Fig. 1. The effect of microcurrent treatment on chronic spinal pain.

the Profile of Mood States, a standardized psychological test of depression, anxiety, fatigue, and cognitive function, among other factors.

It was found that the CES treated patients improved significantly on every measure following three weeks of CES treatment. Neither the sham-treated patients nor the placebo control patients showed improvement on any area measured. These results are given in Fig. 2, where it can also be seen that the patients who received open clinical treatment following the double-blind phase of the research, all at self chosen current intensity settings, actually fared better than those who received the pre set, subsensation level treatment, as would be expected.

A large clinical practice in Southern California chose to complete their research with the open clinical protocol [24]. Again, patients received CES treatments, one hour per day for three weeks. All tests and measures were as described above. They halted the study after the first 20 patients had completed it to see what the results had been. These results can be seen in Fig. 3. The researchers were so impressed that they decided to run the study for an additional 12 months, and are in that process as of this writing.

Researchers at the Louisiana State University Medical School pain clinic are currently implementing the fibromyalgia study double-blind protocol [25], and several other clinics and hospitals are reviewing the protocol for possible participation.

3.3. Research in headaches

Perhaps the earliest US study on headache was done as a Masters Degree thesis at North Texas State University in Denton. In that double-blind, placebo-controlled study, 18 migraine headache patients were divided into three groups of 6 each. 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 [26].

In another study of migraine headaches, this time a doctoral dissertation research project, 36 patients were assigned to biofeedback (BF), CES, or biofeedback combined with CES. Eight treatment sessions of 15 minutes each were given over a two to three week period. The patients measured the frequency-times-intensity of headaches daily during the eight days of therapy, then over a one month, a two month and a three month period following the treatments.

There was no difference between the groups at the end of the eight treatment sessions, but a steadily increasing cumulative improvement took place over the three month period following the study, as shown in Fig. 4. The biofeedback group had an accumulative improvement of 70% while the combined BF/CES group, the group that did best over all, had an accumulative improvement of 400% by the end of the third month [27].

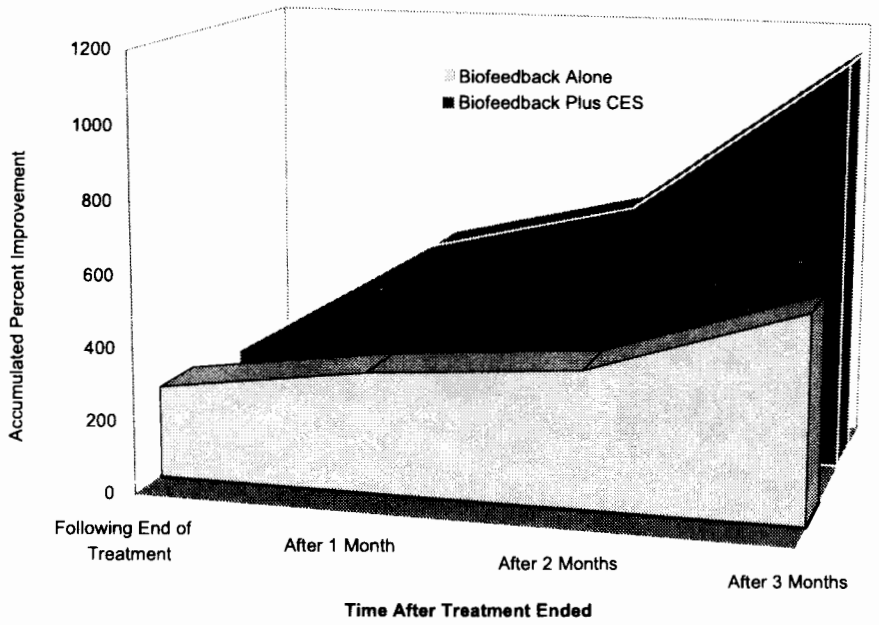

Fig. 4. Frequency of migraine headaches, times intensity.

3.4. Research on dental pain

In a double-blind dental study, 50 patients were divided into two groups, 30 receiving CES and 20 receiving sham CES treatment. 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 4 of 7 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 [30].

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. 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.

A serendipitous, but not surprising finding was that all patients reported feeling more relaxed than usual while in the dental chair [31].

3.5. Chronic pain, type unspecified

In a study of the neurochemistry of depression, CES researchers found that among the patients in their study were 14 who were listed as unresolved chronic pain patients, and 9 other chronic pain patients who considered their condition hopeless. Following two weeks of daily CES treatment, given 20 minutes a day, the 23 chronic pain patients reported a significant reduction of 44% or more in their pain intensity [32].

In a survey of clinicians who use the Alpha-Stim CES device in their pain practice, it was reported that 260 of 286 chronic pain patients (91%) reported significant relief following CES treatments. Among those treated for headaches, 136 of 151 patients (90%) reported significant reduction in headache pain, and 245 of 259 patients (95%) who reported pain related muscle spasms reported significant relief [33].

4. Studies of anesthetic equivalency

There have been two studies that assessed the equivalency of CES to various types of anesthetics. In a rather straight forward study in which he compared CES with various concentrations of N_2O, Stanley gave a group of 90 urological patients and 30 abdominal surgery patients either 75%, 62.5% or 50% N_2O alone or a similar concentration of N_2O plus CES. After 20 minutes of

treatment, patients were given a painful stimulus with a Kocker 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 N_2O by approximately 37% at each level, being between 0.3 and 0.4 MAC in analgesic potency when combined with N_2O. The authors also found that the CES group experienced prolonged analgesia after recovery of consciousness [34].

In a somewhat more elaborate study, CES equivalency to the narcotic fentanyl was studied on 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. All patients had anesthesia induced with droperidol (0.20 mg/kg IV), diazepam (0.2 mg/kg IV), and pancuronium (0.8 mg/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 [35].

5. Discussion

While the above studies represent an entire range of study design from open clinical trials to double-blind, placebo-controlled studies, in every instance treatment with CES has been accompanied by a dramatic reduction in the perception of pain in every pain category studied.

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 did find an increase in serotonin and a decrease in cholinesterase [32]. The other 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 [36].

Pozos' animal studies indicate that CES is apparently effective in bringing neurotransmitters back into homeostatic balance when that balance is deliberately disrupted [37]. 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 [38], CES may be effectively putting it back into a pre stress homeostasis, accompanied by a reduction in stress related hormones such as cortisol, which is 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, even in the absence of perceptible pathology, or 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 [39]. It is known that CES stimulates every area of the brain, and therefore would include the area in which the pain neuromatrix is thought to reside [40, 41]. It is too early to speculate on what the effect of that stimulation might be, but if one is found it will almost certainly be a balancing, or normalizing effect on the cerebral cortex.

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 such as fibromyalgia and RSD. 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 the 145 patients studied, among which was a high incidence of whiplash injury, falls, and physical assaults [42].

Again, it is not clear what the effect of CES stimulation of the medulla is, other than that it provides a bilaterally symmetrical stimulus into the area over time, varying only by the treatment parameters chosen in each instance.

Heffernan found that certain types of CES stimulation, applied to the body, reduced the Fast Fourier Transform root mean square (RMS) of the EEG significantly, leveling out the peaks normally found in pain patients, and changing the EEG into the smooth pattern normally found in pain free patients as shown in

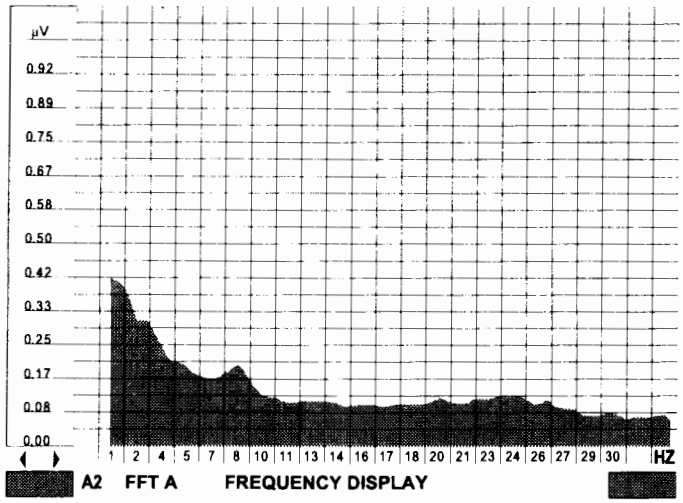

Fig. 5. Fast Fourier Transform of the EEG in a typical pain-free patient. FFT's are based on 2-minute averaged EEG RMS amplitudes on the vertical axis, and EEG frequency on the horizontal axix.

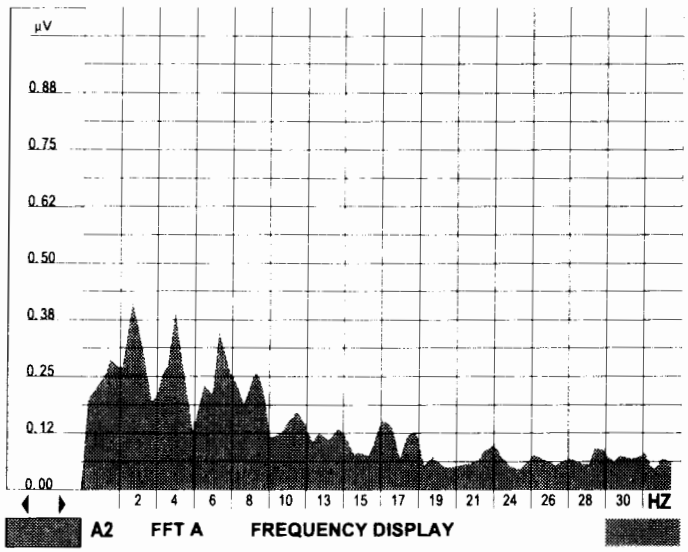

Fig. 6. FFT of a typical chronic pain patient. This patient has degenerative joint disease for more than 2 years causing at least 8 hours of pain daily.

Figs 5, 6 and 7. The patients rated their pain as significantly reduced coincident to the spectral smoothing of the EEG [43]. He also found a significantly concentrated chaos correlation dimension in the EEG following CES suggesting a heightened organization of a formerly less organized EEG in pain patients. This also was accompanied by a reduction in pain and stress symptoms [44].

Many pain clinics across the United States, and now the world, are using the Alpha-Stim 100's CES capability in addition to its available probe and self-adhesive electrodes which are used at or near pain sites on the body of their patients. The use of CES with pain patients is increasingly being supported by the outcome of well-designed research protocols. It's proven efficacy in controlling the anxiety, depression and insomnia ubiquitous in pain patients is a significant added benefit. Side effects are rare, primarily minor self-limiting problems, such as headaches (1 in 450) and electrode burns (1 in 811). As a cost effective, non-medication treatment for the reduction of pain, especially in chronic pain patients, cranial electrotherapy stimulation usage can only increase as practitioners be-

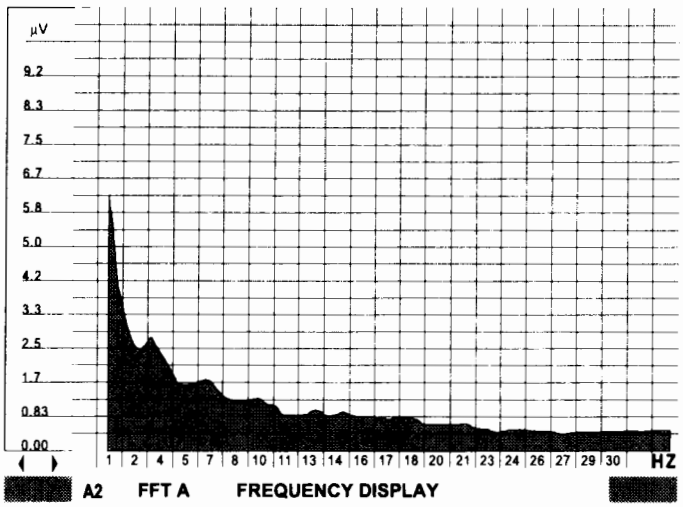

Fig. 7. FFT of the EEG of the same patient in Fig. 6 following 10 minutes of Alpha-Stim CES treatment.

come more aware of its existence, efficacy, safety, and ease of use.

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