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 application in rehabilitation medicine in the United States dating back roughly 1970. As a recognized non-pharmacological 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 injury 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 not so its stress reducing effects when anxiety and depression are reduced below critical levels. Modern theories of a pain neuromatrix in the cerebrospinal fluid may provide an additional basis for understanding CES mechanisms in the control of pain-related disorders.

1. Introduction

Cranial Electrotherapy Stimulation (CES) is an application of a small amount of current, usually less than one milliamperic, 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 ethnically 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 1990 [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 first 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 products so the plants had to be abandoned. It continued to be used in treatment, however, with many facilities by 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

Whatarot and his coworkers presented their paper "Effects of CES therapy on spinal cord injured patients in the acute phase of injury" 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 sham CES or sham CES one-hour daily for three weeks. Monday through Friday. They were pre and posttested 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 presenter reported that CES was...
subsequently employed in the hospital treatment proto-
col, with the physical therapists, especially, comment-
ing that patients had much better morale during muscle
ease training when they used a CES device during the
daily mandatory passive exercise sessions. They com-
pleted 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
case clinical presentation of two CHI patients, the
major focus being on their post-traumatic amnesia and
subsequent cognitive deficits. It was found that follow-
ing 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 sec-
ond 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 depres-
sion in these patients, a side issue was the seizure dis-
orders 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 cen-
ter 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 re-
searchers designed a study to see whether or not “telev-
trosleep” actually put patients to sleep. Among 15 pa-
tients in this open clinical trial were two patients suffer-
ing 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 char-
acter during the passage of current, and eventually com-
pletely eliminated, as measured by EMG [16].

In another study, researchers found that in at least
some types of patients, muscle tremor can be associ-
ated 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 for-
merly 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 mea-
sured by the Minnesota Multiphasic Personality Inven-
tory and tremor was measured with the Lafayette In-
strument Steadiness Tester. It was found that benz-
diazepines, 25 mg. t.i.d. and 30 mg. b.i.d. 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 spas-
tic cerebral palsy, aged 2.5 months to 15 years, CES
or sham CES was given twice a day for ten minutes
each for six weeks in a crossover design. The
results were evaluated on the Mullen Gross Motor Rat-
ing Scales I, II, and III, and the Advanced Gross Mo-
tor 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 physica-
therapy is superior to conventional treatment alone [18].

In the latest such study to appear in the CES litera-
ture, 10 patients diagnosed with minimal cerebral dys-
function, cerebral palsy and spastic quadriplegia were
given either occupational therapy (OT) alone, CES
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-Stat 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-Stat 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 at larger medical centers and for open clinical trials at 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, 30 Hz, one 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 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 psychiatrist 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 stringency 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 50 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 physical 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
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 subthreshold 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-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 90% by the end of the third month [27].
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 (57%) 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 660 dental procedures over a 12-month period. 76% of the patients reported a 99% 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 biochemistry 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 266 chronic pain patients (98%) 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 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 a similar concentration of N₂O plus CES. After 20 minutes of
treatment, patients were given a painful stimulus with a Kremer clamp clamped on the second racket 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<sub>O</sub> by approximately 37% at each level, being between 0.3 and 0.4 MAC in anagracea potency when compared with N<sub>O</sub>. 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 anesthesis induced with propofol (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, no studies that looked for this did not find it, although one did find an increase in serotonin and a decrease in cholecystokinin [32]. The other study found an increase of MAA-B in blood platelets and an increased concentration of GABA in the blood following CES treatments, but did not find an increase in seratonin, dopamine or beta-endorphins in the blood [36].

Potts' 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 pulling us 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 effect 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 occull damage in the lower medullary sensory and motor pathways in complex regional pain syndromes such as fibromyalgia and RSD. These studies suggest that bilateral spinohalamic and corticospinal deficits, with a conspicuous ipsilateral hemisensory and hemisomatic pattern, contralateral cranial nerve X dysfunction, and lack of other consistent cranial nerve findings are compatible with dysfunction of lower medullary sensory and motor pathways [38]. 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 simulation 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.

Hoffman found that certain types of CES simulation applied to the body, reduced the Fast Fourier Transform root mean square (RMS) of the EEG significantly, lowering to discernable levels found in pain patients, and changing the EEG into the smooth pattern normally found in pain free patients as shown in...
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-
more aware of its existence, efficacy, safety, and ease of use.

References
The use of cranial electrotherapy stimulation in the management of chronic pain.