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Low Level Brain Stimulation for Anxiety: A Review of 50 years of Research and Supporting Data

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Abstract

Cranial electrotherapy stimulation (CES) is the use of low level electrical stimulation to the brain for anxiety, insomnia and depression. It has been used and researched in the USA since the early 1960s. More than 40 research studies have been reviewed for this article, plus the results of a survey of physicians who evaluated its effectiveness as a treatment for anxiety and stress in 500 of their patients. An analysis is also given of patient perceived treatment effects from surveys on warranty cards submitted by 500 people who had been prescribed CES units for the treatment of their anxiety, and/or anxiety related disorders.

The data supports the conclusion that CES may be an underutilized, but safe and effective non-drug treatment for anxiety.

Low Level Brain Stimulation for Anxiety: A Review of 50 years of Research and Supporting Data

Cranial electrotherapy stimulation (CES) is a USA Food and Drug Administration recognized treatment of anxiety that involves the passage of microcurrent levels of electrical stimulation across the head via electrodes placed bilaterally on the ears. Most CES devices stimulate with either sinusoidal or modified square waves, at from 0.5 to 100 Hz, and from 0.1 to 1.0 mA in intensity. Stimulation duty cycles range from 20% to 80%, with most devices stimulating on a 50% duty cycle. The devices are about the size of a deck of cards.

The recommended treatment protocol for the treatment of anxiety is typically the application of CES for 20 minutes to one hour daily for two to three weeks, and then on an as-needed basis. The patient adjusts the current to a comfortable level. By the end of the first week of treatment symptoms have usually subsided significantly or resolved completely. CES is a non medication therapy, that may be used alone as the sole treatment for anxious patients.

CES is the name suggested by the FDA for this medical treatment that arrived in the USA in the early 1960s as "electrosleep." It had been developed in Russia as a treatment for insomnia; a way of inducing sleep. It was thought that by significantly reducing the current from that used in electroanesthesia, one could induce a relaxing, natural sleep. (1) Much of the early CES research in the USA involved the determination of which wave shapes, pulse rates, and current intensities were necessary to induce sleep in patients. They soon discovered that one could not reliably use electrosleep parameters to induce sleep in patients. (2-7)

Serendipitously, it was found that while CES was not putting them to sleep, psychiatric patients who had been previously refractory to treatment, experienced significant improvement in symptoms of depression and anxiety, among several others. (8-12).

Like most new medical treatments, CES was attacked from all sides. It had to be proved that stimulation of such small intensity – below sensation threshold in blinded studies – could even get into the brain (13-15), that it evoked changes in the EEG (16-20), and that it was effective whether or not the patient

went to sleep. (21) In addition it had to be shown that its effect was present above and beyond the patient's level of suggestibility (22), and that it was effective over and beyond any placebo effect, which was never found in studies designed to measure for it. (10, 23-24)

Among the more than 150 CES human and animal studies published in the USA few reported the means and standard error of the means required for meta-analyses of the studies. Three such analyses were performed, however, all concluding that CES was unquestionably effective for the treatment of anxiety. (25-27)

One possible mechanism of action was elucidated at the University of Tennessee Medical Center by Pozos, and his coworkers, who completed five studies on groups of canine subjects in which psychoactive medications were used to disrupt the neurotransmitter balance in their brains, causing Parkinson like symptoms. Once all drugs had been removed from their blood half the animals that were then provided normal kennel routine came back to normal within 4 to 7 days. The half that were given CES in addition to their normal kennel routine, returned to normal behavior in 2 to 8 hours suggesting that CES rebalances neurotransmitters. (28)

Very early on in the USA, CES began to be used in treating the substance abstinence syndrome in which patients suffering from various addictive substances suffered intensively from anxiety, depression and sleep disturbance. Because that group has proven susceptible to cross addiction to psychoactive medications, and because they are also more resistant to the effects of such medications than are non addicted patients, CES soon became a treatment of choice in both inpatient and outpatient treatment programs for this group of patients. (29-33)

In 1976, the USA Congress passed the Medical Device Amendments Act, giving FDA control over medical devices. Subsequently, the FDA called CES before its Neurology Panel in 1978, and the Panel recommended that it be approved immediately for the treatment of anxiety. They recommended that it be called back later to assess the several other uses that had become apparent in the published literature. The FDA decided that if electrosleep did not actually put people to sleep it should be called something else, and they developed "cranial electrotherapy stimulation" as the new rubric for its use in America.

The FDA also decided to leave CES as a prescription device, for the treatment of anxiety, depression and insomnia, the approved indications for CES as of this writing.
To date, there have been over 126 published studies and reviews based on human subjects, and 29 animal studies. (34) The most recent human studies have shown CES to be a significantly effective treatment for fibromyalgia (35-36), reflex sympathetic dystrophy (37), and for pain treatment. (38) In the fibromyalgia and RSD studies, in addition to pain, patient anxiety was measured with standardized psychological measures and found to improve significantly, with a strong correlation found between the patients' level of anxiety and self rated pain scores.

Physician Ratings of CES Treatment Results. A researcher polled 47 physicians to ascertain treatment results of 500 patients for whom the physicians had prescribed CES treatment. The physicians reported that among previously treatment resistant anxiety patients, more than 93 percent had achieved significant improvement in their anxiety symptoms with the use of CES. (34)

Patient Self Report of CES Treatment Results. Recently, the self report records of 500 patients suffering from various anxiety states were examined to see how they rated the effects of CES treatment on their symptoms. Patients whose physicians prescribe the Alpha-Stim CES device (Electromedical Products International, Inc., Mineral Wells, Texas, USA 76067; www.alpha-stim.com) routinely submit warranty cards in which they can complete a survey wherein they volunteer information regarding their diagnosis, the length of treatment prior to submitting the warranty card, and their self evaluation of the treatment results.

From more than 3,000 warranty cards most recently analyzed, the cards of 500 anxiety patients were selected for evaluation, in the order they were received. Of the 500 cards selected, 311 (62%) were submitted by female patients. The ages ranged from 3 years to 89 years of age with the breakdown as shown in table 1, where it can be seen that patients were prescribed treatment with CES throughout the life span, with the majority falling between the ages of 40 and 59.

Table 1. Age range of patients using CES devices, as reported on warranty cards

Age Range	3-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89
Number	13	37	69	159	119	62	33	8
Percent	2.6%	7.4%	13.8%	31.8%	23.8%	12.4%	6.5%	1.7%

Patients rated their improvement in each of the improvement categories provided, as shown in table 2.

Table 2. Treatment outcome following CES treatment of anxiety

Improvement	None	1 - 24%	25 – 49%	50-74%	75-100%	Significant (25%+)
Nr. Reporting	24	63	110	156	147	413
% Reporting	5%	13%	22%	31%	29%	82%

Many of the cards were sent in following one or two days of treatment, but several were sent in following 12 months of treatment and two were sent in following 156 weeks of treatment. When a correlation was run between the length of treatment and the results of treatment, it was found that while some patients responded at the 100% improvement level within the first week, and at least two patients had received no treatment benefit from three months of treatment, there was an overall correlation of .63 between the length of CES use and improvement in anxiety, which had strong statistical significance ($p<0.001$).

While 473 of the cards analyzed listed anxiety as the primary diagnostic factor, 39 listed stress, but did not name anxiety as such. Twenty-seven listed both stress and anxiety. For purposes of the present evaluation, stress and anxiety are combined. Only 175 (35%) listed anxiety alone, while 100 (20%) listed anxiety and depression, 195 (39%) listed anxiety and pain, and 30 (6%) listed anxiety and sleep problems. In addition, many listed other anxiety related states and those, along with their self rated treatment results are shown in table 3.

Table 3. Analysis of treatment outcome for treatment of anxiety related states

Anxiety Related State	Number Responding	Age Range	Sex	Weeks Treated	Mean Improvement	Significant Improvement
Panic Disorder	14	30-69, Mean = 49	50% Female	.14 – 52, Mean= 9	45%	42%
OCD	5	13-41, Mean = 27	60% Female	1 – 16, Mean = 6.25	68%	100%
Bi-Polar	9	33-61, Mean = 49	89% Female	3 – 24, Mean = 10	71%	88%
PTSD	8	39-58, Mean = 51	63% Female	Mean = 9	55%	71%
Cognitive Problems (ADHD)	23	7-65, Mean = 37	61% Female	.14-52, Mean=9	62%	81%
Phobias	9	31-72, Mean = 52	78% Female	.29 – 24, Mean = 8	49%	60%
Total	54	7-72, Mean = 37	63% Female	.14-52, Mean = 9	64%	73%

The figures shown in table 3 include many patients who had their CES device for a week or less. On inspection of the data for the group reporting panic disorder, it was found that those who had used CES for three weeks or less reported insignificant treatment results, while those using it 10 weeks or more reported a 99% remission of symptoms. When the treatment times for the combined group shown in table 3 were examined, it was found that those using their device one week or less prior to submitting their warranty card reported an average 49% improvement, while those using their device from two to three weeks reported a 62% gain, and those using it four weeks or more reported 64% improvement. Among the last group of patients who had their CES device for 4 weeks or more before sending in their warranty card, 81% claimed significant treatment response of 25% or greater, the standard of a successful outcome commonly used in medication studies.

The treatment effect size, evaluated as the binomial effect size, is equal to the percent improvement claimed, and as shown in tables 2 and 3, the mean effect size for all 500 patients reporting was .62 (e.g., 62% improvement in symptoms). When the smaller groups of patients with special types of anxiety related disorders was broken out, the effect size among those suffering from panic disorder was .45, that of OCD patients, .68, those with bi-polar disorder .71, and so on for PTSD (.55) ADHD (.62), and phobias (.49). The overall mean effect size for the combined smaller groups was .64. Those can be compared with the standard effect size ratings of .10 for small, .30 for medium and .50 for large. (39)

Discussion

There has now been 50 years of experience with CES in the USA as a non medication treatment for anxiety, yet it has never reached mainstream status as a treatment modality by members of the medical and allied healthcare professions. That is most likely due to the fact that no medical school in the USA teaches CES treatment as part of its curriculum, and none of the CES companies has had sufficient staff to visit physicians' offices in the ubiquitous manner of pharmaceutical representatives. Therefore, there has been no formal post graduate inservice or updating of physicians regarding the literature on CES as a treatment modality except for an occasional lecture at a medical symposium. However, there were over 50 Alpha-Stim CES exhibits at medical conferences in 2005 compared to less than 10 in any year previously.

Nonetheless, when physicians who had prescribed CES were asked, those responding were enthusiastic about its effectiveness, as are the great majority of CES experienced patients themselves, as reported on their warranty card responses and the testimonials they freely submit to www.alpha-stim.com.

Patient response on warranty cards can perhaps be seen to be even more significant in that the Alpha-Stim CES device offers a 30 day period in which a patient can return the unit at if it is proving to be ineffective. Less than 1% of patients return them for this reason, and almost none are returned by patients who use them in the suggested manner in the treatment of their anxiety, 20 minutes to one hour a day for the first three weeks, then as needed to prevent symptoms from returning. The fact that the cost of such devices can range from $500 to $900 USD makes the pronounced tendency of patients to hold on to and continue using them even more impressive.

Also noteworthy is that among the more than 6,000 patients who have been involved in CES research studies in the USA, and among the 500 patients who submitted the warranty cards as reported here, there has been no significant, negative side effect reported from the use of CES. Or as the National Research Council reported to the FDA when asked to evaluate the safety of CES, “Review of these reports reveals that significant side effects or complications attributable to the procedure are virtually nonexistent.” (40)

It is likely that CES will receive greater attention from medical practitioners as more knowledge is gained about its use and usefulness as a drug free treatment of anxiety, and anxiety related disorders.

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