

Cranial Electrotherapy Stimulation: Treating the Brain with Electrons for Pain and Stress-Related Disorders

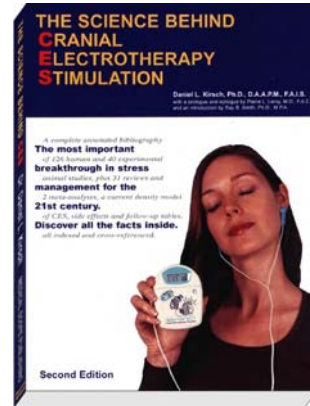
Daniel L. Kirsch, PhD, DAAPM, FAIS

33 Years of Experience in Electromedicine
Chairman, Electromedical Products International, Inc.

- > Former Clinical Director of the Center for Pain & Stress-Related Disorders of Columbia-Presbyterian Medical Center at the College of Physicians and Surgeons of Columbia University of the City of New York
- > Diplomate, American Academy of Pain Management
- > Fellow, American Institute of Stress
- > Member, International Society for Neuronal Regulation
- > Consulting Editor, *Journal of Neurotherapy*
- > Electromedicine Dept. Editor, *Practical Pain Management*
- > Honorary Member, Inter-Pain (Germany/Switzerland)
- > Member, Presidents Council, University of North Texas
- > Pain, Stress and PTSD Consultant to US Army and VA



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Cranial Electrotherapy Stimulation (CES)

Easy 4-Step Procedure:

1. Wet Electrodes
2. Place on Ear Lobes
3. Turn on CES Device
4. Set to Comfortable Current for 20 Minutes to One Hour



The application of low level current, (usually <1 mA) applied across the head for medical or psychological conditions, or just as an aid in relaxation

FDA authorized by Rx for anxiety, depression and insomnia

Also used for fibromyalgia, ADD/ADHD, PTSD,

CRPS (RSD), phantom limb pain, other pain syndromes

Qualitative Results “What to Expect from CES”

Most people report feeling:

Happier,

Their Bodies are

More Relaxed,

Their Minds are

More Alert,

and They Feel Younger, More Energetic



Dr. Saul H. Rosenthal

Psychiatrist and CES Researcher Reported:

Calm, Relaxed Sensation

Activation of Alertness

Euphoric Tranquility

Not Worrying

Bright and Happy

Increased Energy

Improved Sleep

No Confusion, Memory Loss or Disorientation

Dr. Saul H. Rosenthal

Typical Comments from Patients:

“As if I have been given a happy pill.

Sort of a floaty, smiley feeling, very pleasant.

This is quite a change of moods.”

“Anxiety about capability seems reduced.”

“Smiling for no reason.”

“As though I have almost been conditioned not to worry.”

“Although I feel depressed, it is nothing like

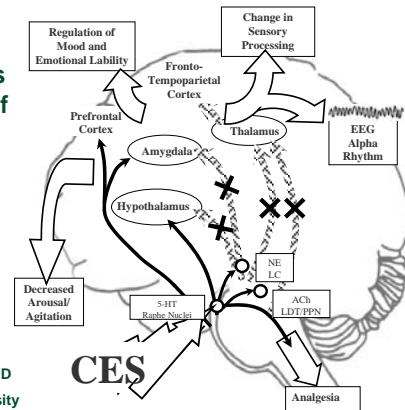
I would expect from past experience,

even though the problem is large.”

Michael Hutchison
Author of the book Megabrain Wrote:

"My body immediately felt **heavier**,
as if I was sinking down into myself.
[Then] I realized I was becoming **extremely relaxed**.
...Things are very, **very clear**.
My body was no longer heavy, but **very light, full of energy**.
The feeling was one of **openness, clarity**,
as though I had been wearing sunglasses for weeks
and had suddenly taken them off.
I couldn't help but feel that
this is the way we're supposed to be all the time."

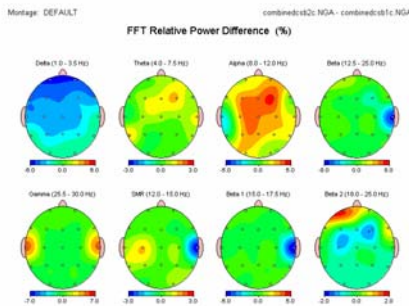
Proposed Mechanisms of Actions of CES



James Giordano, PhD
Georgetown University

QEEG Changes in 30 Subjects Treated with 20 Minutes of CES.
There is an Increase in Alpha and a Decrease in Delta Activity.
Blue = decrease Red = increase

Courtesy of Richard Kennerly, University of North Texas Ph.D. dissertation



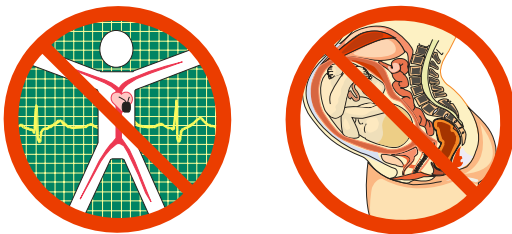
Adverse Effects from CES

From 126 human studies
encompassing 6,007 people
with 4,541 receiving active CES treatment:

9 myogenic headaches (0.20%, 1:506)
5 cases of skin irritation (0.11%, 1:910)

These are mild and self limiting.

Primary Contraindications



Embryofetal Effects on Rats

Little and Patterson, 1996

844 fetal rats had 1 hour/daily CES throughout their pregnancy at 10, 100, or 1,000 Hz, 1 volt, 125 µA via ear tag electrodes.

Autopsy revealed no congenital anomalies.

- ✓ More pregnancy resorptions and fewer offspring in all groups, but only significant in the 1,000 Hz group.
- ✓ Average fetal weight and brain weight were inversely proportional to frequency.
- ✓ Behavior resembled CES in humans, even in this aggressive species; treated rats were not as active as the controls, so the decrease in fetal weights may be because their food intake was lowered.

Conclusion: CES may be embryolethal in the very early stages of pregnancy and might cause some miscarriages, but there is no evidence of fetotoxic effects.



Topics of Scientific Research on CES

Number of Pivotal Scientific Studies:

CES is FDA approved for anxiety, depression, and insomnia

42 Anxiety + 1 Phobia
 26 Depression
 27 Insomnia
 10 stress

Topics of Scientific Research on CES

Number of Pivotal Scientific Studies:

for brain functions	pain	and other applications
3 attention deficit disorder (ADD)	4 anesthesia	2 bronchial asthma
3 cerebral palsy	3 dental	1 gastric acidity
2 closed head injuries	2 fibromyalgia	1 labor
9 cognitive dysfunction	5 headaches	2 sex offenders
3 learning and memory	8 muscle tone/movement/tremor	3 suggestibility
3 reaction time, vigilance	13 pain	
	1 rehabilitation	

Research Methodology of 86 Pivotal (out of 126) Studies of CES

- 35 Double-Blind Placebo-Controlled
- 9 Single-Blind
- 15 Controlled Study
- 6 Crossover
- 22 Open Clinical Trial
- 2 Retrospective Study
- 3 Case Study
- 13 Follow-up

Beta-endorphins

↑ 98% in plasma
 219% in CSF

Serotonin

↑ 15 – 40% in plasma
 50 – 200% in CSF

From research by neurosurgeon C. Norman Shealy, MD

Electromyogram (EMG):

- ♦ ↓ with recovery to normal in 15 minutes
- ♦ ↓ in Mm spasticity in pts with hemiplegia and paraplegia
- ♦ ↓ frontalis Mm
- ♦ ↓ maintained 1 week post treatment
- ♦ ↑ relaxation
- ♦ involuntary movements in pts with Parkinson's and dystonia musculorum were changed during treatment and eventually completely eliminated
- ♦ ↓ 15.8 μV to 4.5
- ♦ ↓ 38 μV to 3.2
- ♦ ↓ 10.4 μV to 3.8
- ♦ ↓ 8.4 μV to 4.0

Experimental Animal Studies on CES

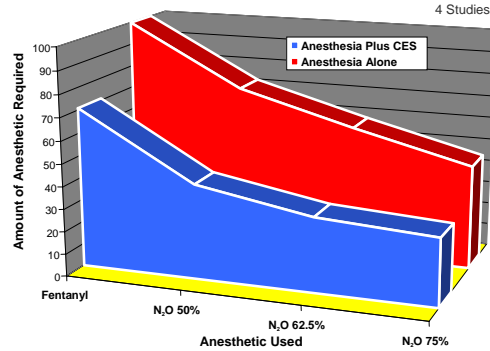
- Rat studies showed as much as a threefold increase in β -endorphin concentration after just one CES treatment (Krupitsky, 1991).
- Blind tests of tail-flick latency (TFL) in rats show a significant increase in analgesic effect of opiates. (Stinus, 1990).

TFL as a % of baseline with drug, and with drug plus CES:

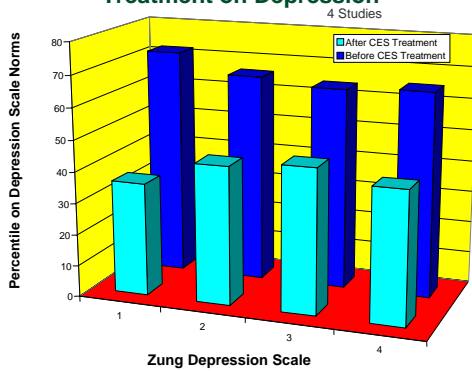
	Drug Alone	Drug Plus CES
morphine	174%	306%
fentanyl	176%	336%
alfentanil	160%	215%
dextromoramide	267%	392%

Results were also obtained after intracerebroventricular injection of morphine (10 micrograms; analgesic effect increase from 152% to 207% with CES) suggesting that CES potentiation of opiate-induced analgesia is centrally mediated.

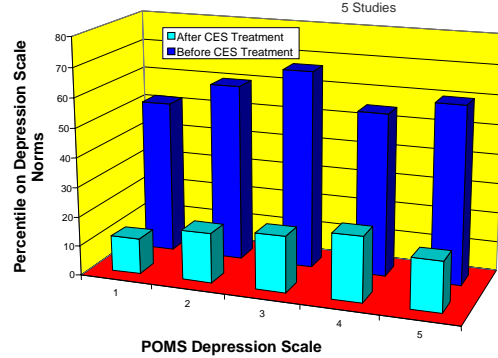
The Use of CES to Potentiate Anesthesia in Surgery



The Effects of 7 to 10 Days of CES Treatment on Depression



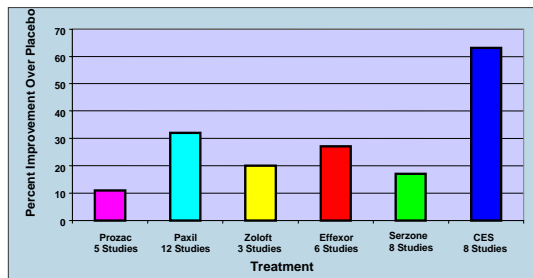
The Effects of 2 and 3 Weeks of CES Treatments on Depression



CES Review: A Safer Alternative to Psychopharmaceuticals in the Treatment of Depression

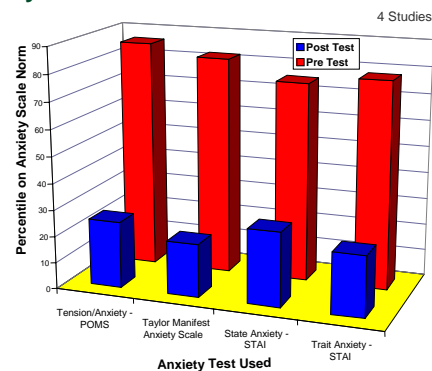
Marshall Gilula, MD and Daniel L. Kirsch, PhD

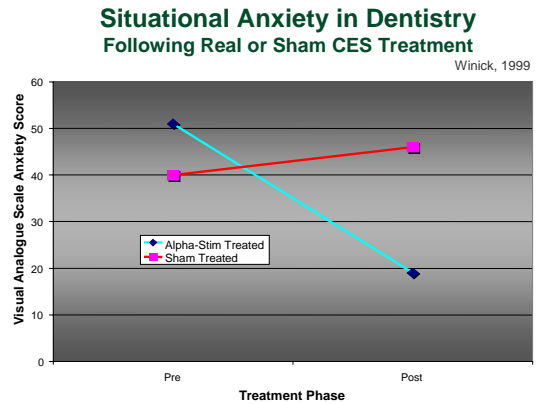
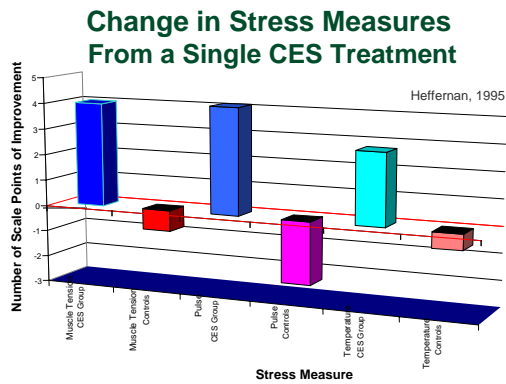
Journal of Neurotherapy, 9(2):2005 downloadable at www.alpha-stim.com



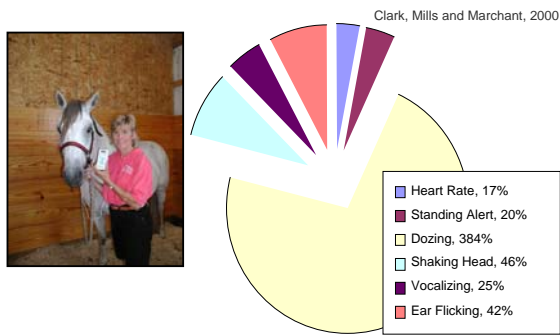
CES is 3x more efficacious than the average SSRI

Anxiety Scores Before and After CES Treatment

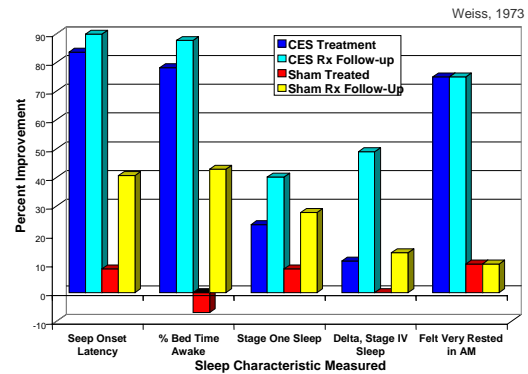




Percent Increase in Relaxation Response of 8 Horses Following 20 minutes of Alpha-Stim Treatment



Response of Insomnia Patients to CES



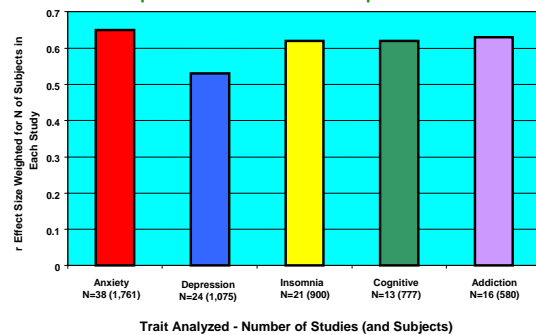
Two Meta-Analyses Reconfirmed the Significance of CES Research for Treating Anxiety:

- ◆ **University of Tulsa** (O'Connor, Presented at the 12th annual meeting of the Bioelectromagnetics Society, 1991)
- ◆ **Department of Health Policy and Management, Harvard School of Public Health** (Klawansky, et al, Journal of Nervous and Mental Disease 183(7):478-485, 1995)

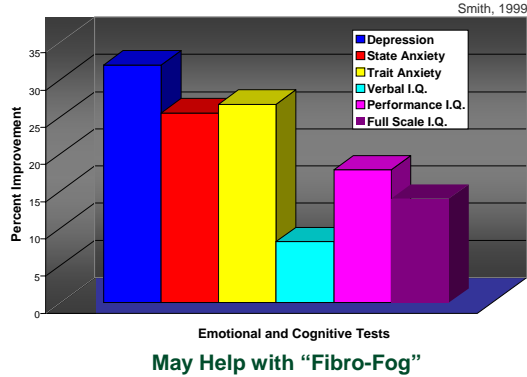
Both Found CES Significantly Effective for Anxiety (P<.05)

Meta-Analyses of the Treatment Effects of CES

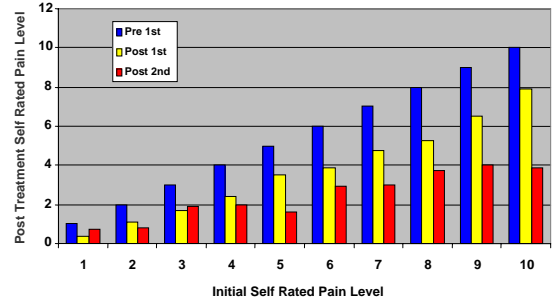
Kirsch et al. -- Chapter 44 in Bioelectromagnetic Medicine, 2004
chapter downloadable at www.alpha-stim.com



Attention Deficit Disorder (ADD)



Patient Response to 1st and 2nd 20 Minute CES Pain Treatments, N = 174



Results Achieved with CES

Based on a Physician Survey of 500 Patients

Condition	N	Worse	No Change	Slight <24%	Fair 25-49%	Moderate 50-74%	Marked 75-99%	Complete 100%	Significant >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%)

Depression: 73% >50% or 52% >75% improved
Pain: 74% >50% or 47% >75% improved
(Average pain reduction from opioid use is 32%)

Results Achieved with CES Technology

Based on a Survey of Patients Reporting Psychological Disorders

Condition	N*	Slight <24%	Fair 25-49%	Moderate 50-74%	Marked 75-100%	Significant >25%
Psychological (all cases)	723	61 (8.44%)	175 (24.20%)	237 (32.78%)	250 (34.58%)	662 (91.56%)
Anxiety (alone)	128	13 (10.16%)	29 (22.66%)	42 (32.81%)	44 (34.38%)	115 (89.84%)
Anxiety (with other)	370	33 (8.92%)	85 (22.97%)	122 (32.97%)	130 (35.14%)	337 (91.08%)
Anxiety/Depression	58	3 (5.17%)	19 (32.76%)	19 (32.76%)	17 (29.31%)	55 (94.83%)
Depression (alone)	53	7 (13.21%)	25 (47.55%)	23 (43.40%)	12 (22.64%)	46 (86.79%)
Depression (with other)	265	25 (9.44%)	61 (22.97%)	93 (35.09%)	82 (30.94%)	236 (89.06%)
Stress	123	6 (4.88%)	30 (24.39%)	39 (31.71%)	48 (39.02%)	117 (95.12%)
Chronic Fatigue	50	3 (6.00%)	30 (60.00%)	10 (20.00%)	7 (14.00%)	47 (94.00%)
Insomnia	163	10 (6.13%)	47 (28.83%)	47 (28.83%)	59 (36.20%)	153 (93.87%)

*Total N = 2500 patients with multiple symptoms. Results of those using Alpha-Stim™ at least 3 weeks before mailing warranty card. Warranty cards are 2500 consecutive cards received as of July 2000.

Depression: 66% >50% or 23 - 31% >75% improved

Results Achieved with CES Technology

Based on a Survey of 2,500 Patients

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%)	741 (38.02%)	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%)

*Total N = 2500 patients with multiple symptoms. Results of those using Alpha-Stim™ at least 3 weeks before mailing warranty card. Warranty cards are 2500 consecutive cards received as of July 2000.

Pain: 61% >50% improved

Results Achieved with CES Technology

Based on a Survey of 2,500 Patients (continued)

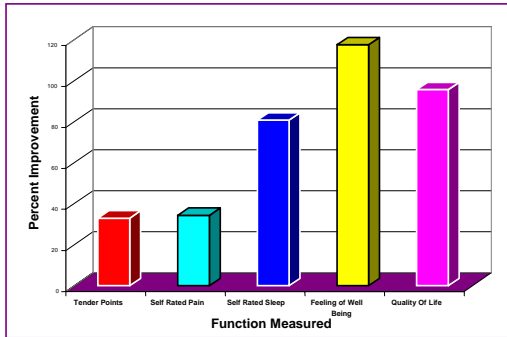
Condition	N*	Slight <24%	Fair 25-49%	Moderate 50-74%	Marked 75-100%	Significant >25%
TMJ Pain	158	17 (10.76%)	60 (37.97%)	60 (37.97%)	21 (13.29%)	141 (89.24%)
Myofascial Pain	62	6 (9.68%)	18 (29.03%)	18 (29.03%)	20 (32.26%)	56 (90.32%)
RSD	55	10 (18.18%)	16 (29.09%)	16 (29.09%)	10 (18.18%)	45 (81.82%)
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%)

*Total N = 2500 patients with multiple symptoms. Results of those using Alpha-Stim™ at least 3 weeks before mailing warranty card. Warranty cards are 2500 consecutive cards received as of July 2000.

Fibromyalgia: 54% - 55 >50% improved

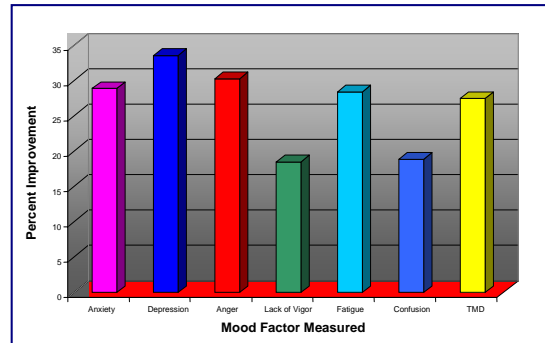
Changes in Fibromyalgia Patients Following 3 Weeks of CES Treatment

Tyers, 2001 (N=19)



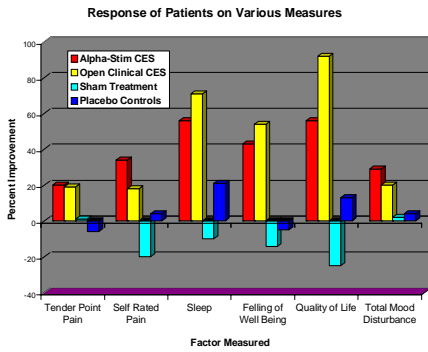
Change in Mood Scores of Fibromyalgia Patients Following CES Treatment

Tyers, 2001 (N=19)



CES Double Blind Fibromyalgia Study Rheumatology

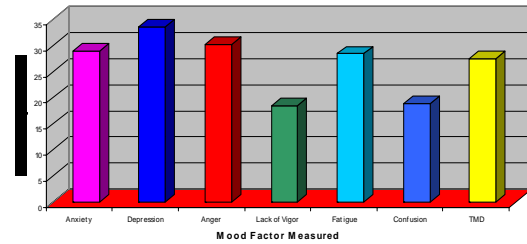
Lichtbroun et al. 2001 (N=60)



CES Double Blind Fibromyalgia Study Rheumatology

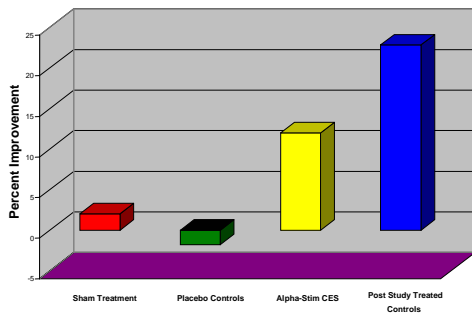
Lichtbroun et al. 2001 (N=60)

Fig 2. Change in Mood Scores of Fibromyalgia Patients Following Alpha-Stim CES Treatment



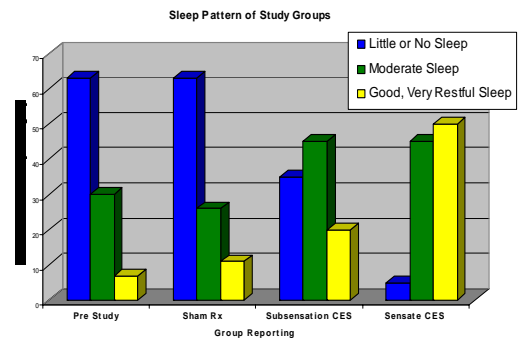
Change in Fibromyalgia Tender Point Pain Scores from Pre to Post Study

Lichtbroun et al., 2001 (N=60)



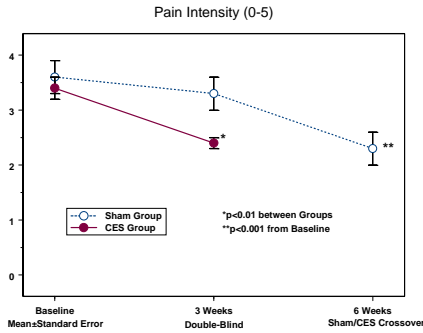
CES Double Blind Fibromyalgia Study Rheumatology

Lichtbroun et al. 2001 (N=60)



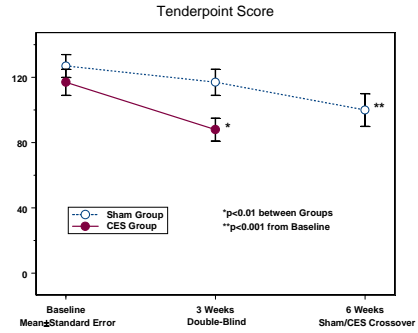
CES Double-Blind Fibromyalgia Study LSU Dept of Anesthesiology

Cork et al. 2004 (N = 74)



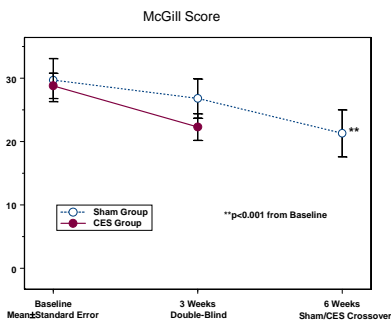
CES Double-Blind Fibromyalgia Study LSU Dept of Anesthesiology

Cork et al. 2004 (N = 74)



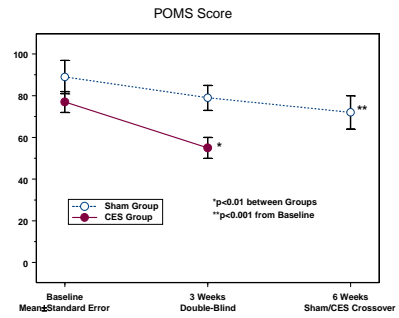
CES Double-Blind Fibromyalgia Study LSU Dept of Anesthesiology

Cork et al. 2004 (N = 74)



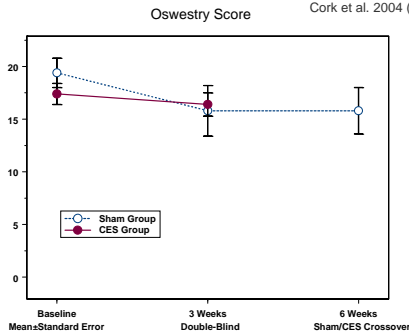
CES Double-Blind Fibromyalgia Study LSU Dept of Anesthesiology

Cork et al. 2004 (N = 74)



CES Double-Blind Fibromyalgia Study LSU Dept of Anesthesiology

Cork et al. 2004 (N = 74)



VA Houston Spinal Cord Injury CES Study

Treating Spinal Cord Injury Pain with Cranial Electrotherapy Stimulation
 - The Pain Relief 2004 Study: A Double-Blind, Randomized, Controlled Trial
 - Michael E. DeLuca, Veterans Affairs Medical Center, Harbor College of Medicine, Dept. of PM&R, Washington, DC; Veterans Affairs Medical Center, University of Texas at Houston, Center for...

PROCEDURE

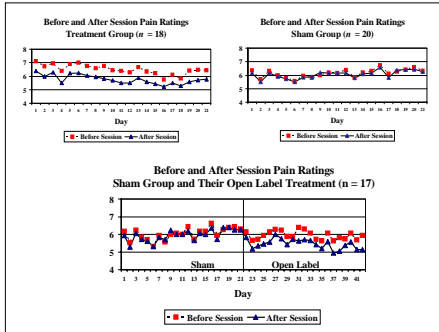
RESULTS

CONCLUSIONS

Based on reported pain reduction per and post each session, the Active CES treatment was found to be significantly more effective than the Sham treatment with a tendency to large effect size (Cohen's d = 1.7). Future studies will be needed to evaluate the long-term effectiveness of CES.

VA Houston Spinal Cord Injury CES Study

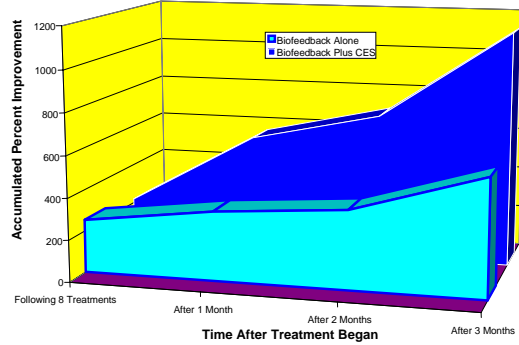
Tan et al., 2006



Figures 1, 2, and 3: Daily Pain Rating for Active CES and Sham CES Groups

Migraine Headaches -- Frequency x Intensity

Brotman, 1989



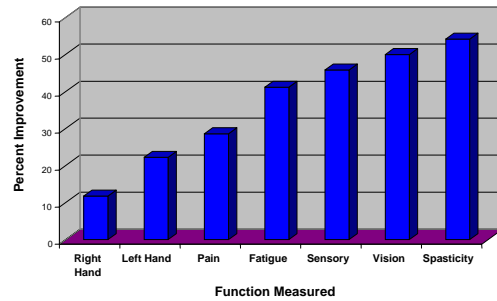
Example of the CES Response in a Patient with Severe Migraine

Courtesy of COL Michael Singer, Walter Reed Army Medical Center



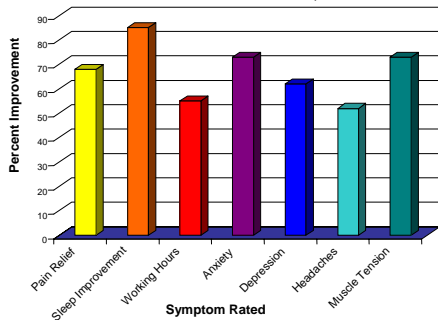
So, stay with it!

The Response of 5 Multiple Sclerosis Patients after 4 Weeks of CES



Improvement in RSD Symptoms and Function Following CES Treatment

Alpher and Kirsch, 1998



Comments on Follow-up from CES Research Studies

FROM PIVOTAL SCIENTIFIC STUDIES:

First Author Year	N	Subject Description	Authors' Comments on Follow-up
Brotman, Philip 1986	36	classical migraine pts	CES group responded significantly better than the other 2 groups over the 3 month follow-up.
Brovar, A. 1984	25	cocaine abusers	No CES patients had returned for treatment, while 50% of the CES refusers and 39% of the controls recidivated in 6 to 8 months.
Fliemenbaum, A. 1974	28	anxiety, depression, insomnia outpatients unresponsive to medication	Those who had beneficial results maintained them throughout the 6 month follow-up.
Hearst, E.D. 1974	28	psychotherapy outpatients	3 patients showed continued improvement for 2 weeks to 2 months.

Heffernan, Michael 1995 20 **generalized stress pts >1 year, unresponsive to medication** 1 week follow-up measures in the CES group showed significant carryover effects in EMG and HR

Magora, F. 1967 20 **A: anxiety, depression, insomnia hospitalized polysubstance abusers, and 9 B: asthmatic children unresponsive to medication** A: Follow-up has continued for 8-12 months after treatment and has revealed no relapse. B: The asthmatic attacks stopped completely in 3 children and 4 months later the children felt well without taking any drugs.

Matteson, Michael 1986 62 **32 CES graduate students, 22 controls** A follow-up measure 2 weeks post study found that 11 of the 13 variables were still significantly improved in the treatment group.

Moore, J.A. 1975 17 **anxiety and insomnia pts** a remarkable improvement" in their symptoms 2 - 3 weeks after CES.

Overcash, Stephen 1999 197 **anxiety outpatients** On 6 - 8 month follow-up, 73% of the patients were "well satisfied with their treatment and had no significant regression or other anxiety disorder.

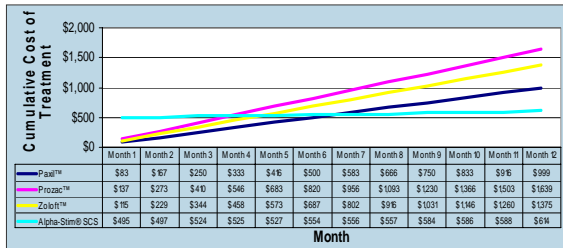
Patterson, M. 1984 186 **hospitalized alcohol and polysubstance abusers** 78.5% were addiction-free (80.3% of drug addicts) 1 to 8 years after CES, with an average time in rehabilitation of only 16 days.

Smith, Ray 1999 23 **psychiatric outpatients with anxiety, depression, ADD** On 18 month follow-up the patients performed as well or better than in the original study.

Weiss, Marc 1973 10 **insomnia patients** All differences found were maintained at the 2 week and 2 year follow-up.

Comparison of Anti-Depressant Drugs with Alpha-Stim SCS (at \$495) CES First Year

Breakeven is at 4 to 6 Months



Cumulative 5 Year Savings Using CES Instead of Drugs

5-Year Device Warranty and Assuming No Drug Price Increases

