The Management of Anxiety, Insomnia, Depression and Pain with Cranial Electrotherapy Stimulation (CES) and Microcurrent Electrical Therapy (MET): Theory and Practice

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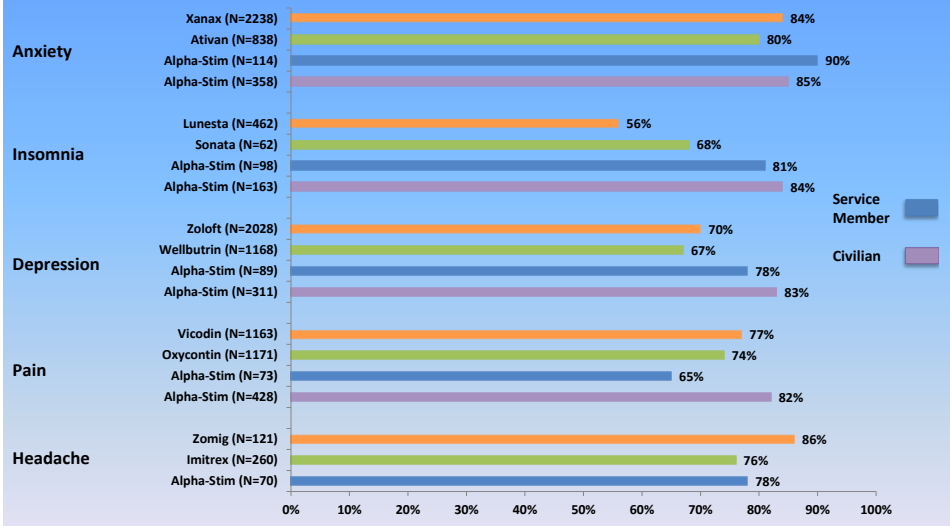
Chief Science and Clinical Officer

Cranial Electrotherapy Stimulation (CES)

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

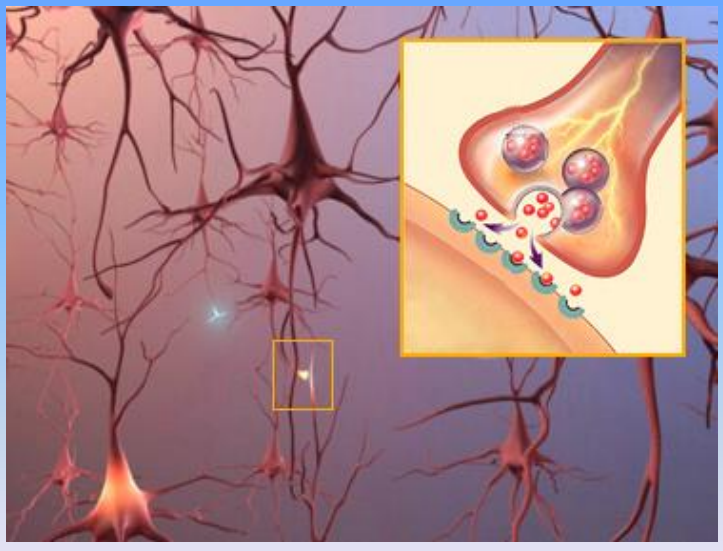
The application of low level current of <1 milliampere applied across the head for treatment of anxiety (including PTSD), depression and insomnia with additional applications being studied.

Patients that Reported a Positive Response: Comparing Alpha-Stim Military Service Member and Civilian Surveys to WebMD Drug Surveys



Kirsch DL, Price LR, Nichols F, Marksberry JA and Platoni KT. Efficacy of Cranial Electrotherapy Stimulation for Anxiety, PTSD, Insomnia, and Depression: US Military Service Members and Veterans Self Reports. *The Army Medical Department Journal*. October-December 2014:46-54.

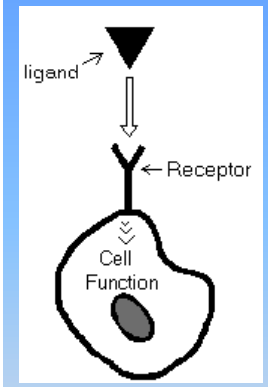
Traditional View of Synaptic Activity



But only 2% of neuronal communication occurs at the chemical synapse.

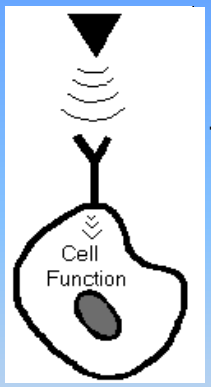
Pert, Candace. Molecules of Emotion: Why You Feel The Way You Feel. Scribner, New York, 1997.

Models of Receptor Activation



19th & 20th Century

The Old Theory: Structural Matching; Chemical/ Molecular Physical Communication



21st Century

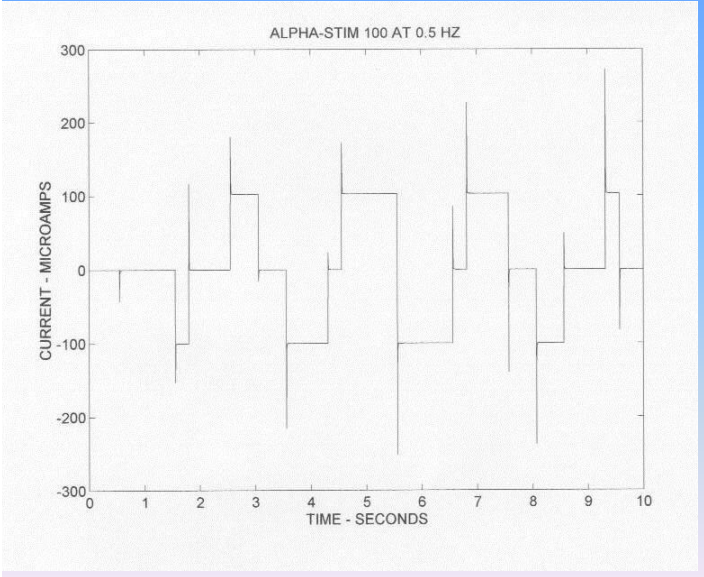
The New Theory: Physical/ Atomic Electromagnetic Communication

The 3D nature of the ligand matches the receptor. Physical proximity induces receptor conformational changes which triggers the cascade of events prompting cell function.

Proximity favors co-resonance of specific bioelectrical signals with frequencies that perfectly match the resonance of the receptor to amplify molecular conformational changes at all steps of the cascade prompting cell function, even from long distances (like tuning in a radio).

Benveniste, J. A fundamental basis for the effects of EMFs in biology and medicine: The interface between matter and function. Chapter 13 in Bioelectromagnetic Medicine. Rosch, P and Markov, M, eds. Marcel Dekker, New York, 2004.

Alpha-Stim® Waveform On Oscilloscope



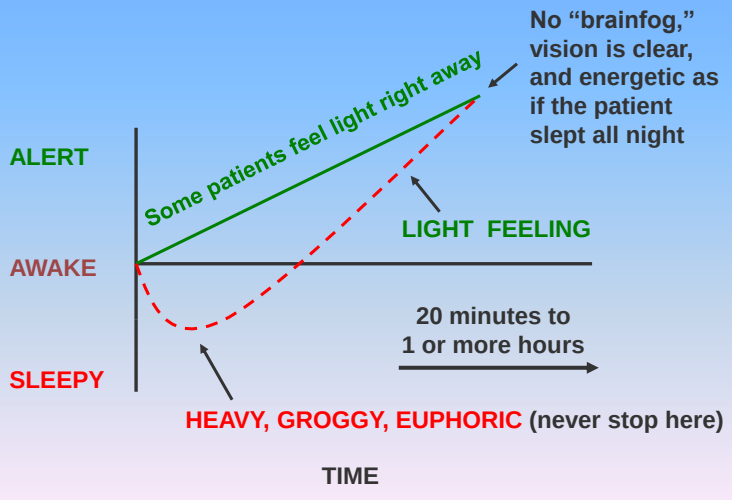
It is the waveform that differentiates devices.

Through periodic, but slow, reversal of the polarization of the DC current, the Alpha-Stim waveform is able to inject a spectrum of low frequencies into the neuronal tissue to match frequencies with different receptors, thus activating them in a way similar to chemical ligands.

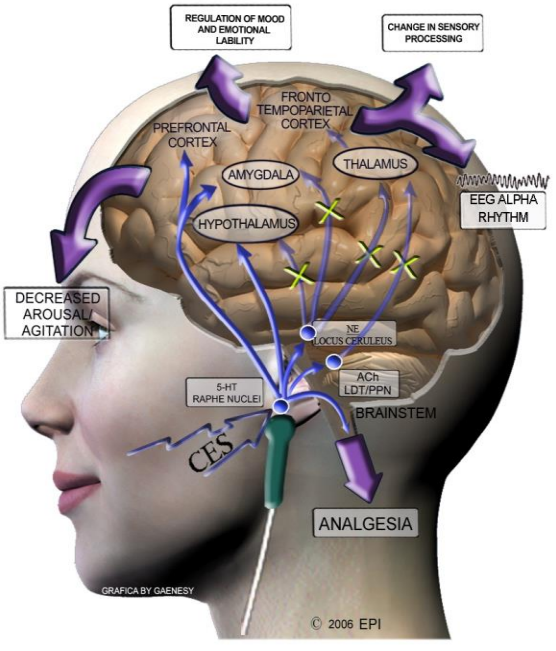
Feelings Experienced During CES Treatment Stages

Dosage equals time inversely proportional to current level.

Therefore, less current requires longer treatment time per session.



Putative Mechanism of CES



CES engages the serotonergic (5-HT) raphe nuclei of the brainstem. 5-HT inhibits brainstem cholinergic (ACh) and noradrenergic (NE) systems that project supratentorially. This suppresses thalamo-cortical activity, arousal, agitation, alters sensory processing and induces EEG alpha rhythm. 5-HT can also act directly to modulate pain sensation in the dorsal horn of the spinal cord, alter pain perception, cognition and emotionality within the limbic forebrain.

Legend:

Blue arrows: inhibitory interactions

Purple arrows: excitatory interactions

X: suppressed pathways/interactions

Ach acetylcholine

LDT laterodorsal tegmental nucleus of the brainstem

PPN pediculo-ponitne nucleus of the brainstem

NE norepinephrine;

LC locus ceruleus,

5-HT serotonin

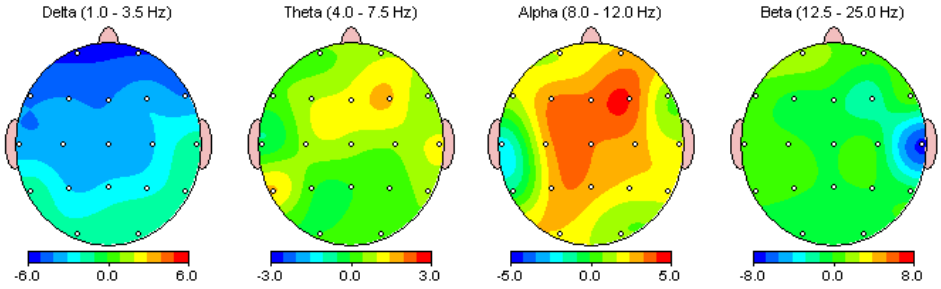
Giordano, James. Illustrating how CES works. Insert in Kirsch, Daniel L. Cranial electro-therapy stimulation for the treatment of anxiety, depression, insomnia and other conditions. *Natural Medicine*, 23:118-120, 2006.

qEEG Changes in 30 Students Treated with 20 Minutes of Alpha-Stim CES

There is an increase in Alpha activity with a simultaneous decrease in Delta.

Blue = decrease Red = increase

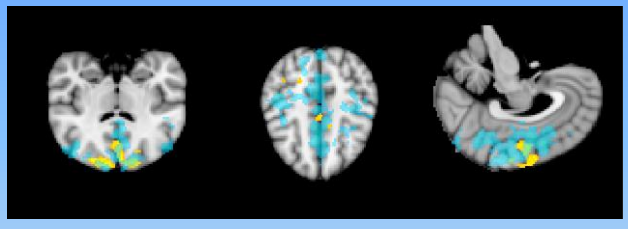
FFT Relative Power Difference (%)



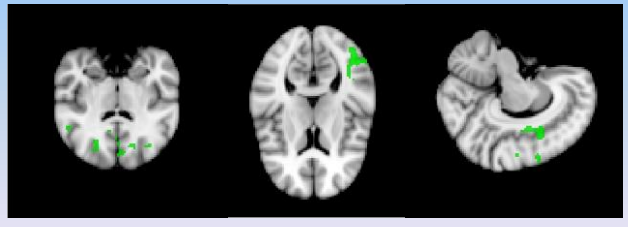
Kennerly, Richard. QEEG analysis of cranial electrotherapy: a pilot study.
Journal of Neurotherapy, (8)2, 2004.
Presented at the International Society for Neuronal Regulation conference, September 18-21, 2003, Houston, Texas

Effects of Cranial Electrotherapy Stimulation on fMRI Brain Activity in the Resting State

Regional deactivation associated with 0.5 Hz (blue)



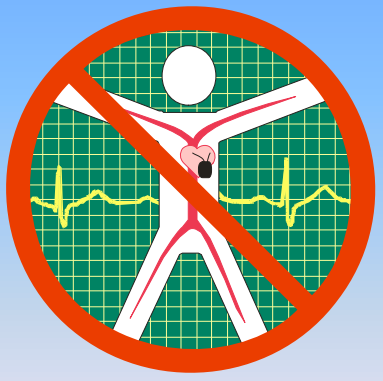
Regions positively associated with current intensity for 0.5 Hz

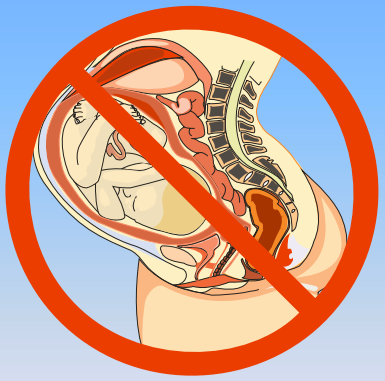


Feusner , Jamie D., Madsen , Sarah, Moody, Teena D., Bohon , Cara, Hembacher, Emily, Bookheimer , Susan Y. and Bystritsky, Alexander. Effects of cranial electrotherapy stimulation on resting state brain activity. *Brain and Behavior*. Pp 1-10, 2012.

Safety Considerations

Primary Contraindications





Adverse Effects from CES

From 144 human studies encompassing 10,556 people where 8,792 received active CES:

9 headaches (0.10%, 1:977)

6 cases of skin irritation (0.07%, 1:1,465)

These are both mild and self-limiting.

If the current is set too high headaches, vertigo or nausea could develop and may last for hours or rarely for days in people with a history of vertigo.

If the treatment is stopped too soon a heavy feeling accompanied by disorientation may persist for hours or even days.

Topics of Scientific Research on CES

Number of Pivotal Scientific Studies on Indicated Uses:

42 Anxiety

27 Insomnia

26 Depression

Research is done independently

Double blinding capabilities

Follow up studies show a durable effect

State (Situational) Anxiety

State anxiety can be effectively treated in a single CES treatment session.

This is demonstrated in medical and dental studies and in mechanistic studies of EEG and fMRI changes from a single CES treatment.

Results will vary based on initial anxiety level, length of treatment, comorbidities and overall patient health.

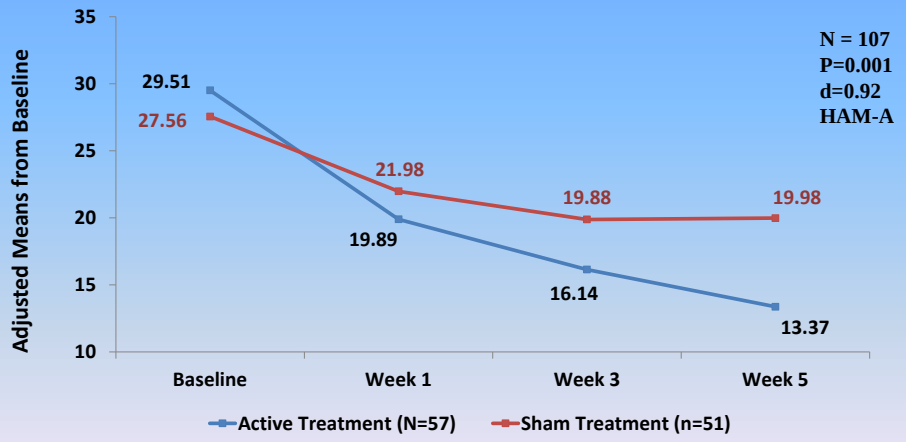
Trait (Chronic) Anxiety

May require up to 6 weeks of CES treatments to see significant reduction in trait anxiety levels.

Treatment outcome may also depend on comorbidities such as depression and insomnia.

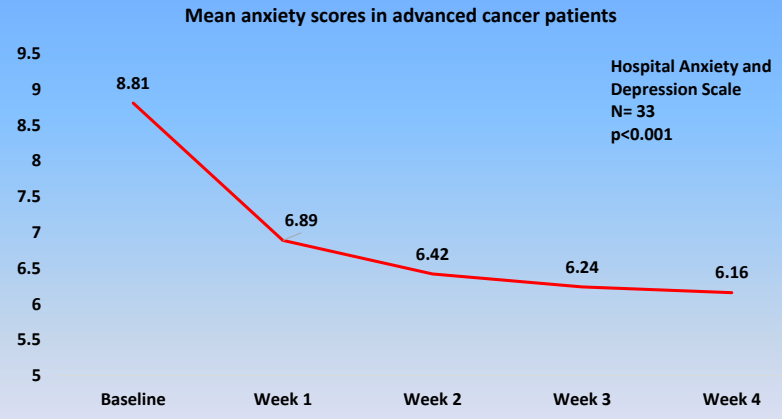
Mean Anxiety Scores

83.7% of the active group reported at least 50% improvement.
The active group reported 3 times more improvement than the sham group.



Barclay TH, Barclay RD. A clinical trial of cranial electrotherapy stimulation for anxiety and comorbid depression. *Journal of Affective Disorders*. 2014; 164:171-177. Presented at the American Psychological Association National Conference, Honolulu, HI, July 2013.

Anxiety Improvement in Advanced Cancer Patients

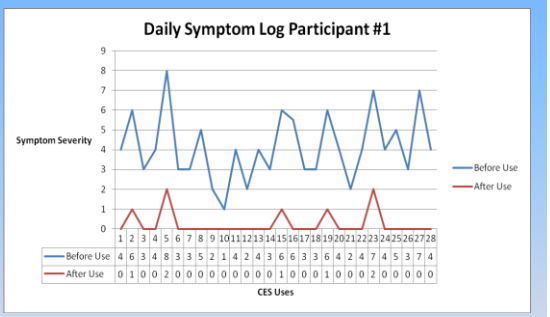


Yennurajalingam S, Kang D-H, Hwu W-J, Padhye NS, Masino C, Dibaj SS, Liu DD, Williams JL, Lu Z, Bruera E. Cranial electrotherapy stimulation for the management of depression, anxiety, sleep disturbance, and pain in patients with advanced cancer: a preliminary study. *Journal of Pain and Symptom Management.* E-published ahead of print, September, 2017.

PTSD in a 54 Year Old Male Veteran

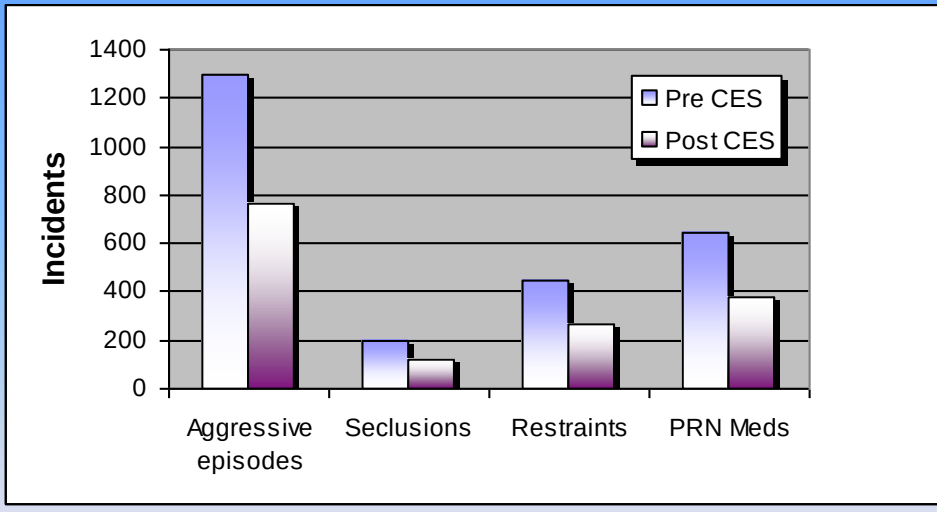
Overall Decrease in Severity by 39% in One Month

PTSD Symptom Scale – Interview (PSS-I)	PRE	POST
PSS-I (Range: 0-51)	34	13
Re-experiencing (0-15)	7	2
Avoidance (0-21)	15	7
Increased Arousal (0-15)	12	4



Bracciano, Alfred G., Chang, Wen-Pin, Kokesh, Stephanie, Martinez, Abe, Meier , Melissa & Moore, Kathleen. Cranial Electrotherapy Stimulation in the Treatment of Posttraumatic Stress Disorder: A Pilot Study of Two Military Veterans. *Journal of Neurotherapy,* 16(1): 60-69, 2012.

3 Month Trial with 48 Severe Aggressive Patients



41% reduction in episodes of violence (P<.001); 40% reduction in episodes requiring restraint (P<.001) and seclusion (P<.05), and 42% fewer as-needed emergency medications (P<.01).
The decrease of 271 PRN med doses in 3 months saved >$12,000 for these med expenses alone.

Childs, Allen and Price, Larry. Cranial electrotherapy stimulation reduces aggression in violent neuropsychiatric patients. *Primary Psychiatry*, 14(3):50-56, 2007; Presented at American Psychiatric Association annual meeting, 2007.

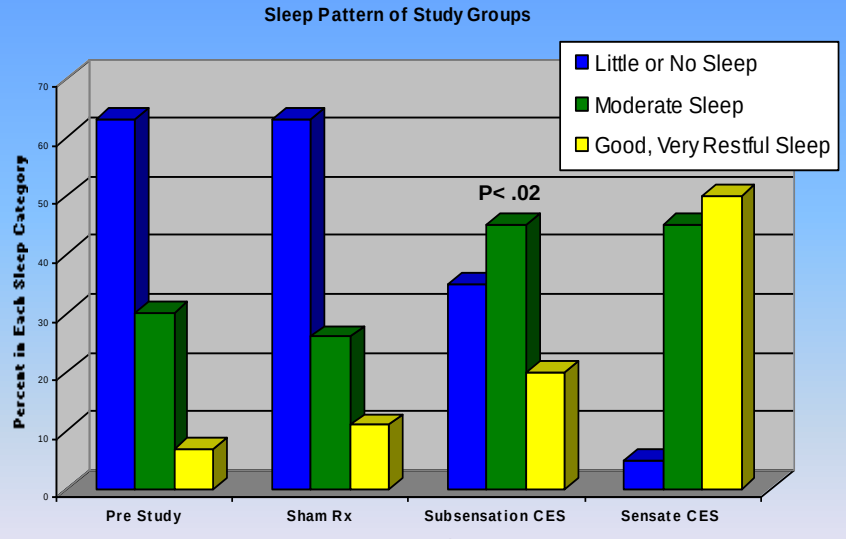
Insomnia

Insomnia patients usually see results after one treatment.

Or it may take up to 4 weeks of treatment, especially if insomnia is associated with depression.

Recent study completed at Walter Reed showed an average increase of +43 minutes of sleep after only 5 treatments.

3 Week RCT of CES for Insomnia in Fibromyalgia Patients



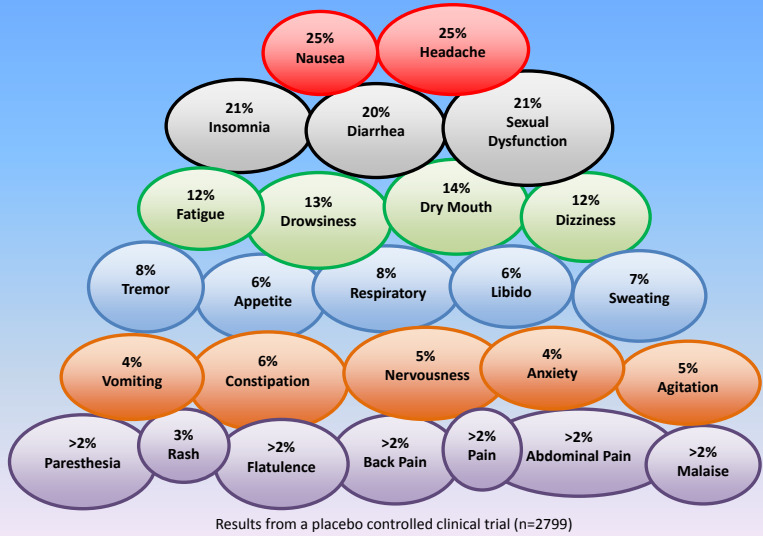
Lichtbroun, A.S., Raicer, M.M.C. and Smith, R.B. The treatment of fibromyalgia with cranial electrotherapy stimulation. *Journal of Clinical Rheumatology*. 7(2):72-78, 2001.
Presented at the 15th Annual International Symposium on Acupuncture and Electro Therapeutics, Columbia University, New York, October 1999.

Depression

Expect a minimum of 3 weeks of daily CES treatment before results are seen.

A patient who suffers from anxiety with a depression component will take up to 3 weeks to improve as well.

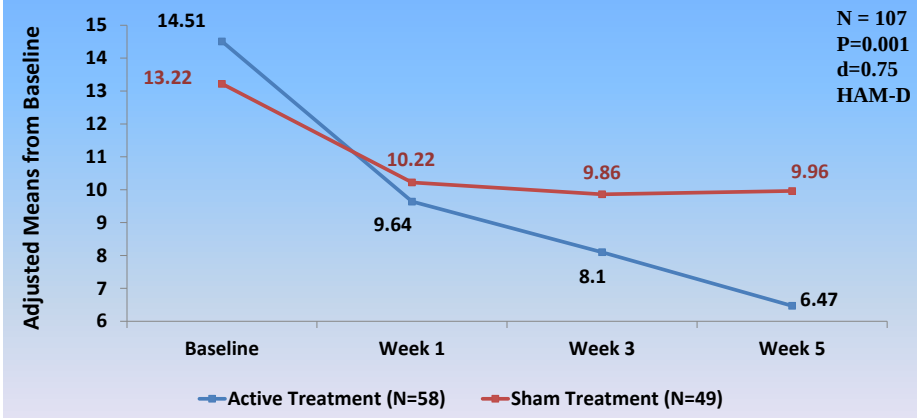
Example of Side Effect Profile for the Popular Antidepressant Zoloft (sertaline)



Results from a placebo controlled clinical trial (n=2799)
As cited by www.drugs.com/sfx/sertraline-side-effects.htm

Mean Depression Scores

82.2% of the active group reported at least 50% improvement.
The active group reported 12 times more improvement than the sham group.



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Depression Improvement in Advanced Cancer Patients

Mean depression scores in advanced cancer patients

Yennurajalingam S, Kang D-H, Hwu W-J, Padhye NS, Masino C, Dibaj SS, Liu DD, Williams JL, Lu Z, Bruera E. Cranial electrotherapy stimulation for the management of depression, anxiety, sleep disturbance, and pain in patients with advanced cancer: a preliminary study. *Journal of Pain and Symptom Management.* E-published ahead of print, September, 2017.

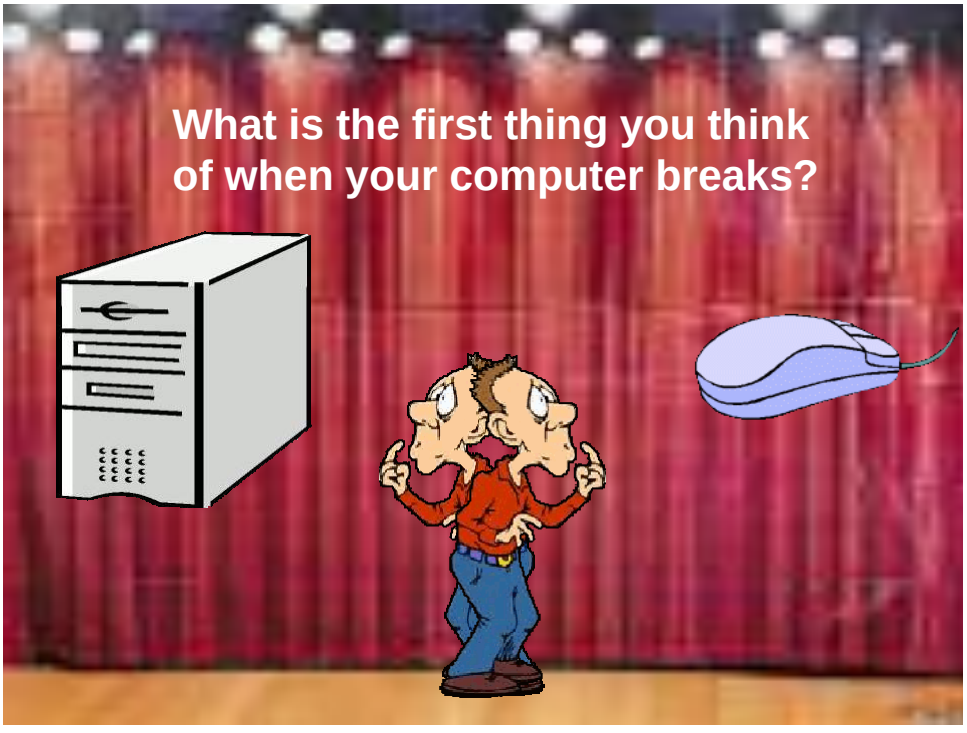
Pain Management

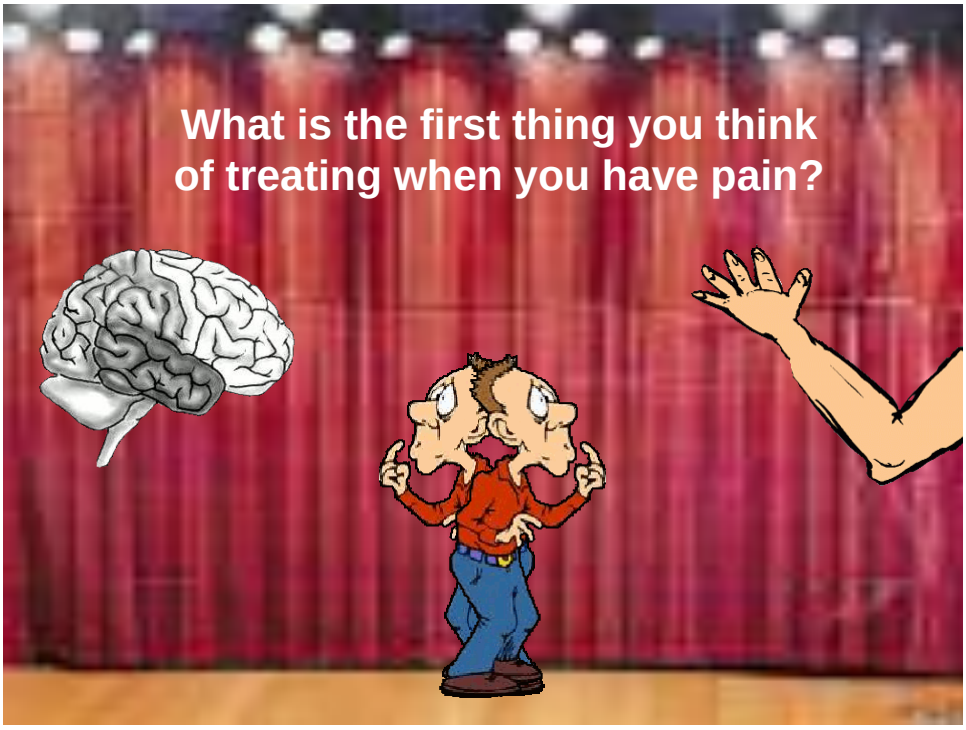
- Acute
- Chronic
- Post-operative

Usually results are seen from the first treatment.

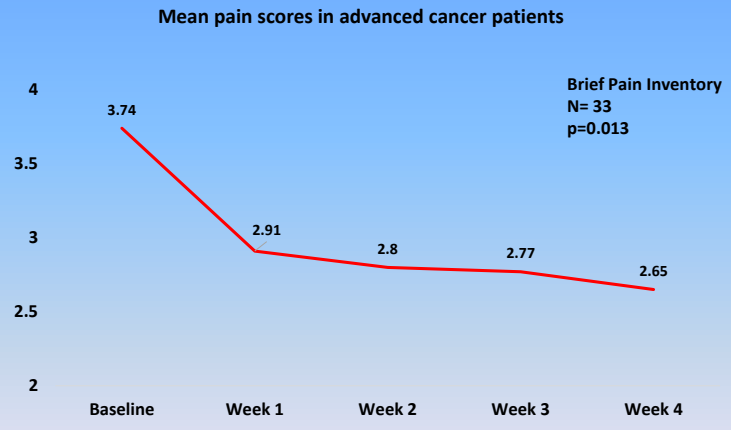
There is no risk of accommodation or addiction.

Pain relief is cumulative with continued use.





Pain Reduction in Advanced Cancer Patients



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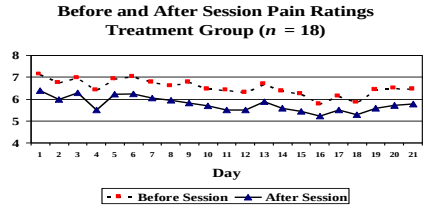
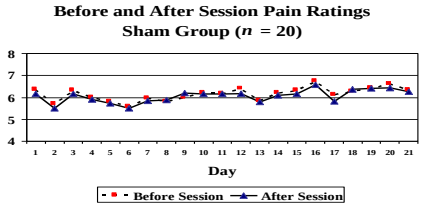
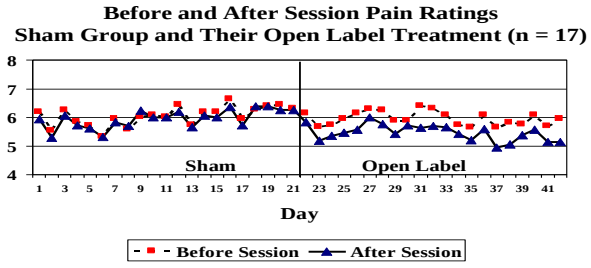
VA Houston CES Spinal Cord Injury Study



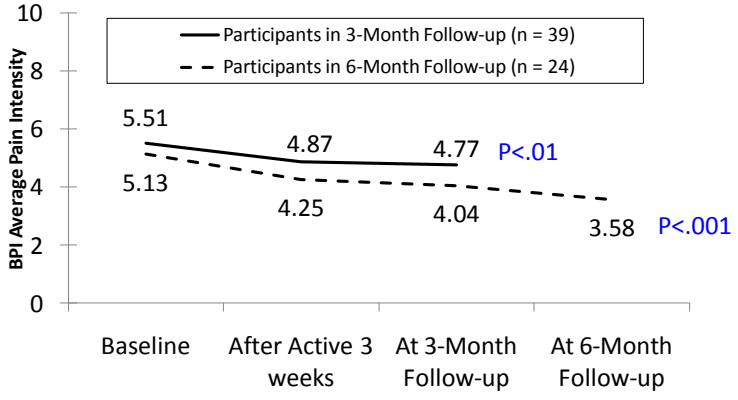




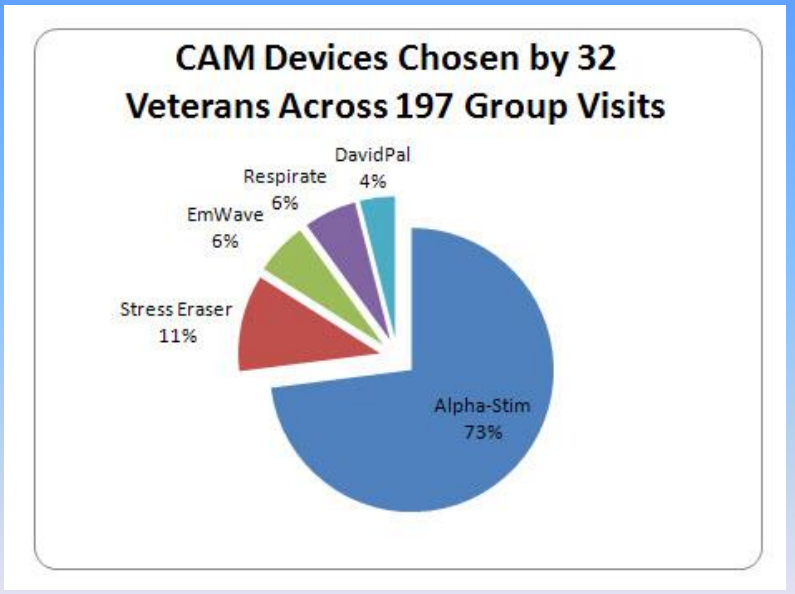
Figures 1, 2, and 3: Daily Pain Rating for Active CES and Sham CES Groups

Tan, Gabriel, Rintala, Diana H., Thornby, John, Yang, June, Wade, Walter, and Vasilev, Christine. Using cranial electrotherapy stimulation to treat pain associated with spinal cord injury. *Journal of Rehabilitation Research and Development*, 43(4):461-474, 2006.

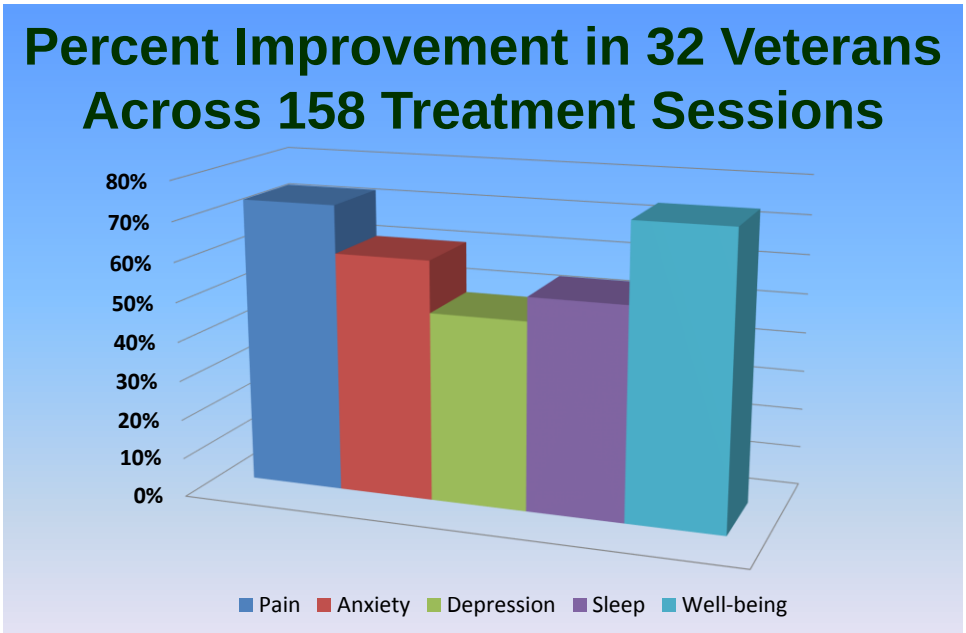
3 Year, 5-Site Spinal Cord Injury Study



Tan, Gabriel, Rintala, Diana, Jensen, Mark P., Richards, J. Scott, Holmes, Sally Ann, Parachuri, Rama, Lashgari-Saegh, Shamsi and Price, Larry R. Efficacy of cranial electrotherapy stimulation for neuropathic pain following spinal cord injury: a multi-site randomized controlled trial with a secondary 6-month open-label phase. *The Journal of Spinal Cord Medicine*, 34(3):285-296, 2011



Tan, Gabriel, Dao, Tam K., Smith, Donna L., Robinson, Andrew and Jensen, Mark P. Incorporating Complementary and Alternative Medicine (CAM) Therapies to Expand Psychological Services to Veterans Suffering From Chronic Pain. *Psychological Services*, 7(3):148–161, 2010.



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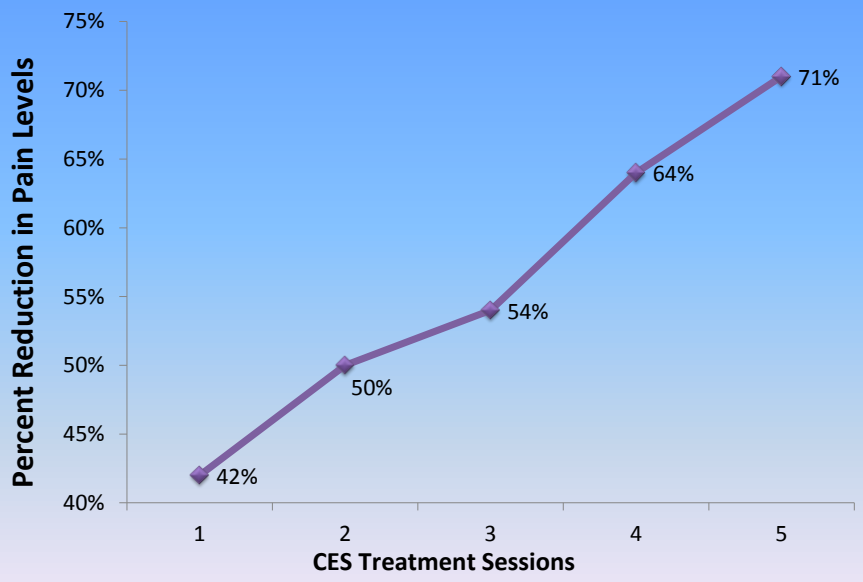
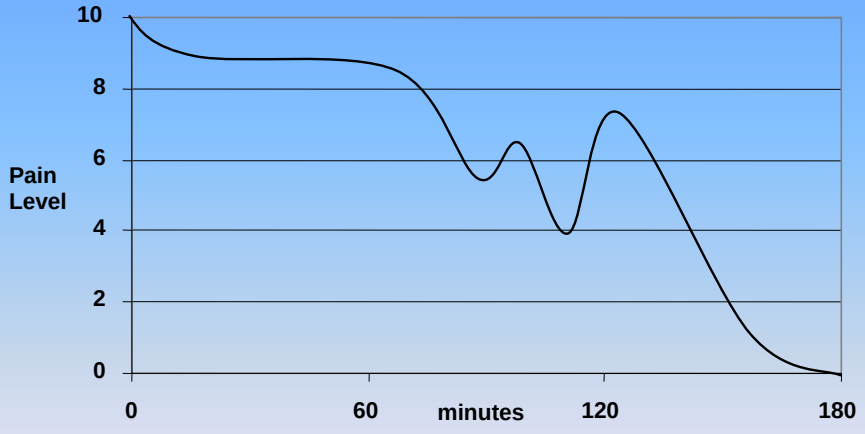
Cumulative Improvement in Pain After 1-5 CES



Holubec, Jerry T. Cumulative Response from Cranial Electrotherapy Stimulation (CES) for Chronic Pain. *Practical Pain Management*, 9(9):80-83, 2009.

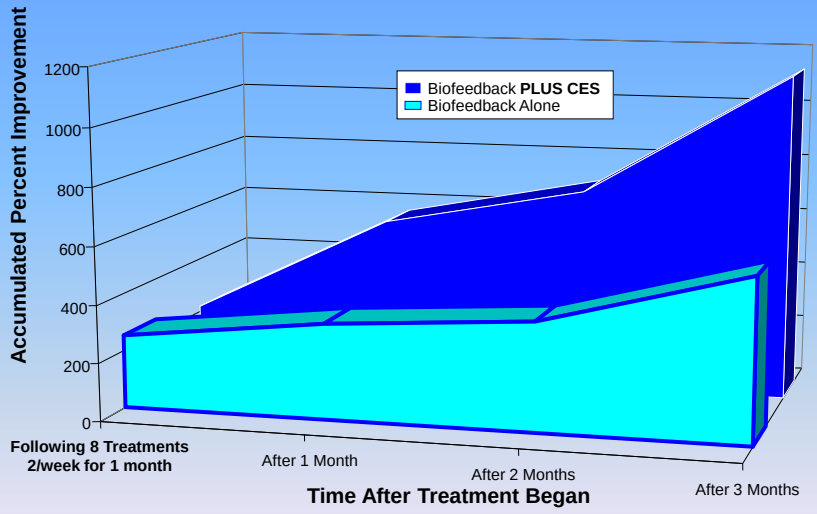
Example of the CES Response Over Time in a Patient with Severe Migraine

Courtesy of COL Michael Singer, Walter Reed Army Medical Center



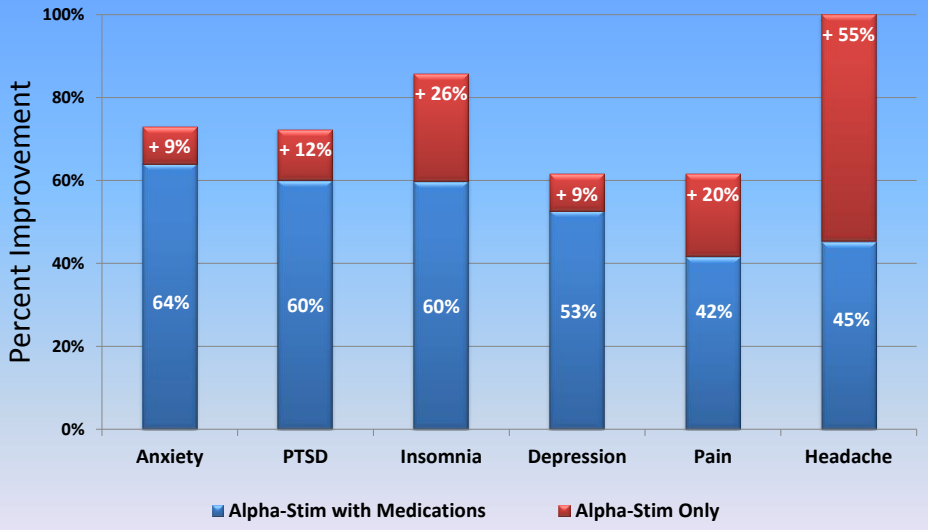
Stay with it!

Migraine Headaches -- Frequency and Intensity
CES Doubles Effects of Biofeedback



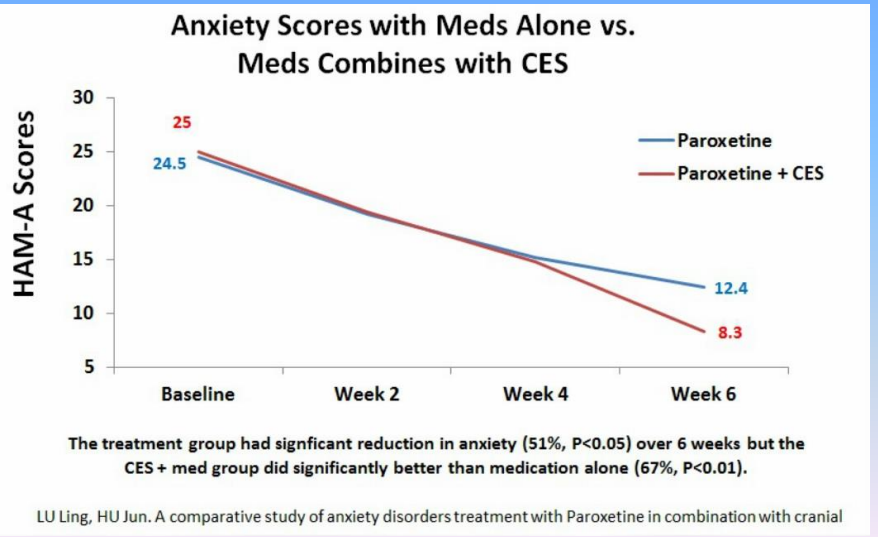
Brotman, Philip. Low-intensity transcranial electrostimulation improves the efficacy of thermal biofeedback and quieting reflex training in the treatment of classical migraine headache. *American Journal of Electromedicine,* 6(5):120-123, 1989. Doctoral dissertation, City University Los Angeles, 117 pages, 1986.

Comparison of Service Members That Used Alpha-Stim With Or Without Medications



Kirsch DL, Price LR, Nichols F, Marksberry JA and Platoni KT. Efficacy of Cranial Electrotherapy Stimulation for Anxiety, PTSD, Insomnia, and Depression: US Military Service Members and Veterans Self Reports. *The Army Medical Department Journal*. October-December 2014:46-54.

Alpha-Stim with Medication



The treatment group had signficant reduction in anxiety (51%, P<0.05) over 6 weeks but the CES + med group did significantly better than medication alone (67%, P<0.01).

LU Ling, HU Jun. A comparative study of anxiety disorders treatment with Paroxetine in combination with cranial

Summary

- **CES is safe**
- **CES is easy to use**
- **CES is proven effective**
- **CES works quickly and lasts**
- **CES is FDA, CE and ISO certified**
- **DoD/VA is using and researching CES**
- **CES is available to help you NOW!**

Practical Protocols

For peripheral pain treatment with microcurrent electrical therapy (MET)…

General Indications

- ✓ **All headaches, including migraine**
- ✓ **Any nerve, muscle, and articular pain**
- ✓ **Sprains, strains, and spasms**
- ✓ **Paresis**
- ✓ **Post-operative pain and scars**
- ✓ **Trigger and Acupuncture points**
- ✓ **Decubitus ulcers and fractures**

  (>1 hour/day at 0.5 Hz and 100 µA)

First, Analyze The Pain

- ✓ Diagnosis is helpful, but not everything
- ✓ Where are all pain/problems located?
- ✓ What position(s) exacerbate them?
- ✓ How bad are they on a 0 - 10 scale <u>right now</u>?
- ✓ Note any obvious signs
- ✓ Note any special symptoms
- ✓ Think holistically, note any related problems
- ✓ Note all scars and old injuries

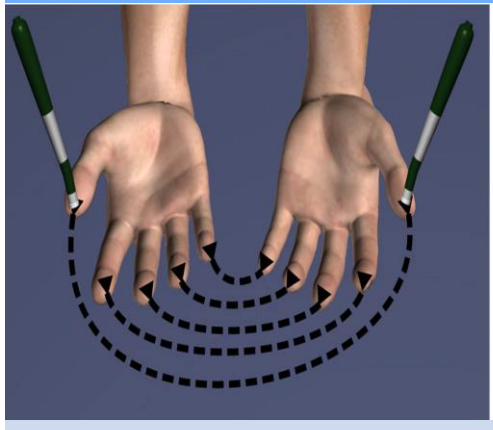
Second, Prepare Device

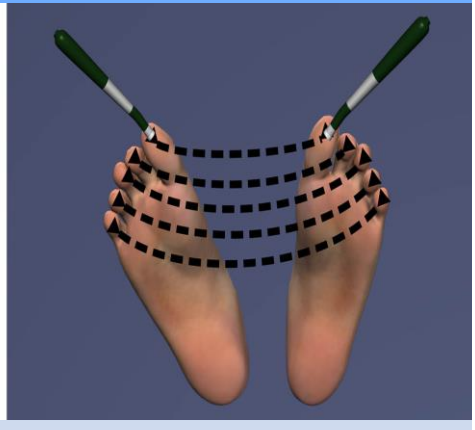
- ✓ **Attach probes to Alpha-Stim**
- ✓ **Place electrodes on probes**
- ✓ **Wet each electrode with Alpha Conducting Solution**
- ✓ **Set frequency to 0.5 Hz**
- ✓ **Use 100 Hz *only* for initial treatment of inflammatory joint disease in remission**
  _i.e._, "dry joint"
  (10 - 20 seconds per site)
- ✓ **Set current to maximum of 600 microamperes, or to a comfortable level on the head**
- ✓ **Set timer for probe**

Basic 5-Step Protocol

1. First treat in a big "**X**" beyond the area(s) of pain
2. Then treat through the areas in three dimensions, like a star (*e.g.,* 2 obliques, A-P, M-L)
3. Treat the opposite side even if it is asymptomatic
4. Always connect both sides (*most important step*)
   - ✓ Press fairly hard
   - ✓ Reevaluate pain about every 1 - 2 minutes ("set")
5. Finish with CES

The 1-Minute Protocol

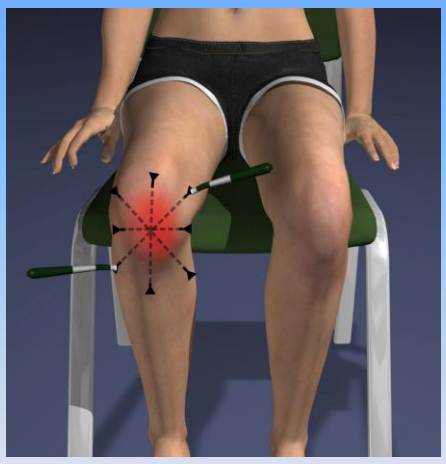




1. This treats the entire UE, neck and shoulders

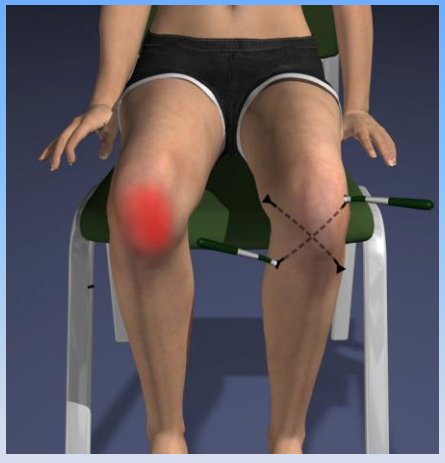
2. This treats the entire LE, pelvis and low back

Example 1: L.E. Pain (knee)



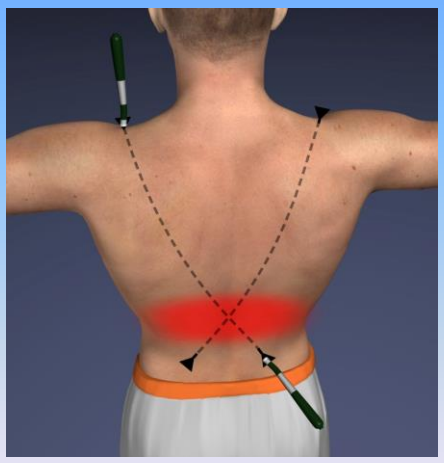
The Standard 2-Minute Protocol

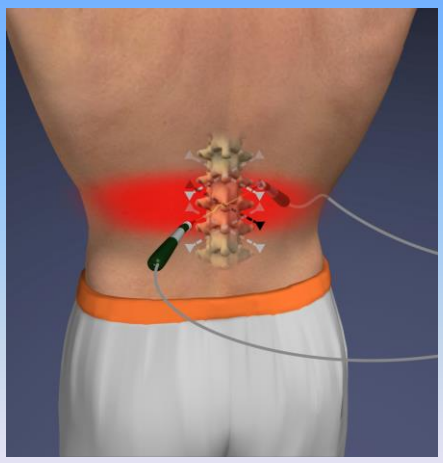
Example 1: L.E. Pain (knee)



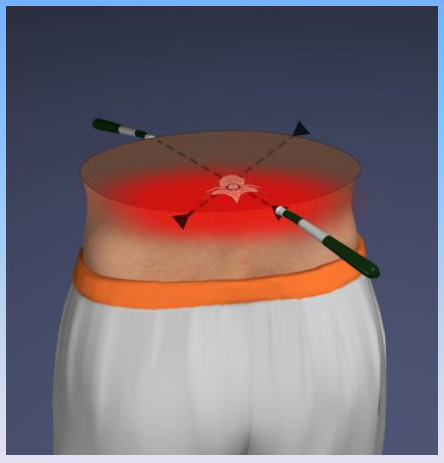
The Standard 2-Minute Protocol

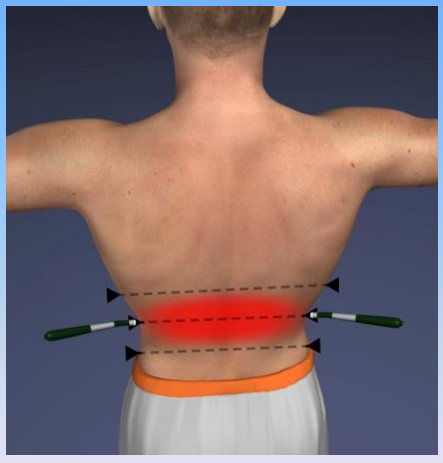
Example 2: Back Pain



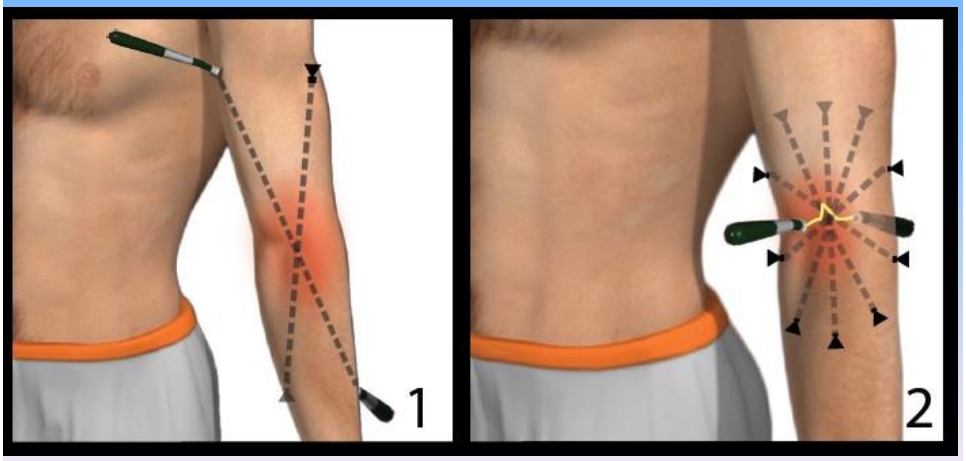


Example 2: Back Pain

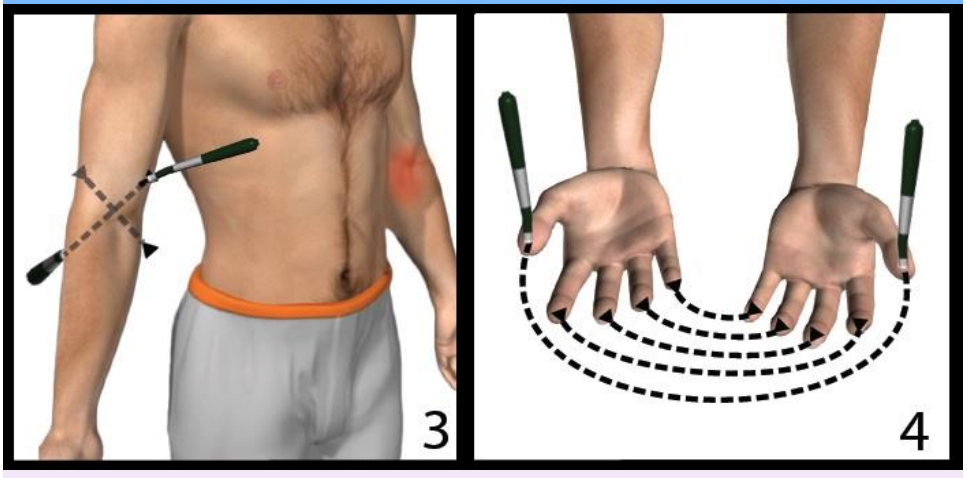




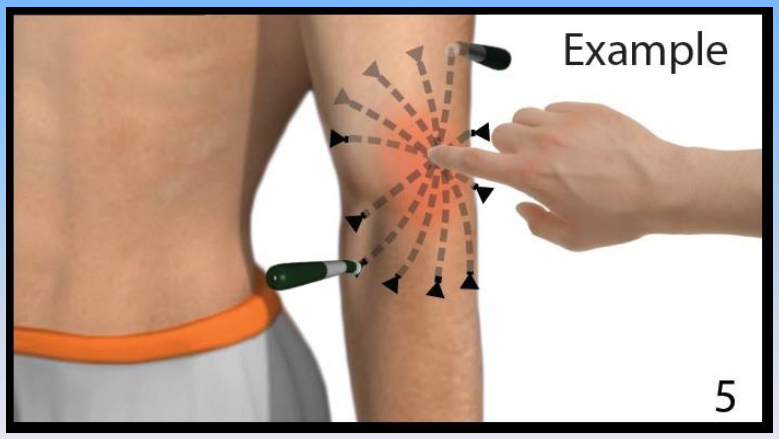
Example 4: Elbow Pain



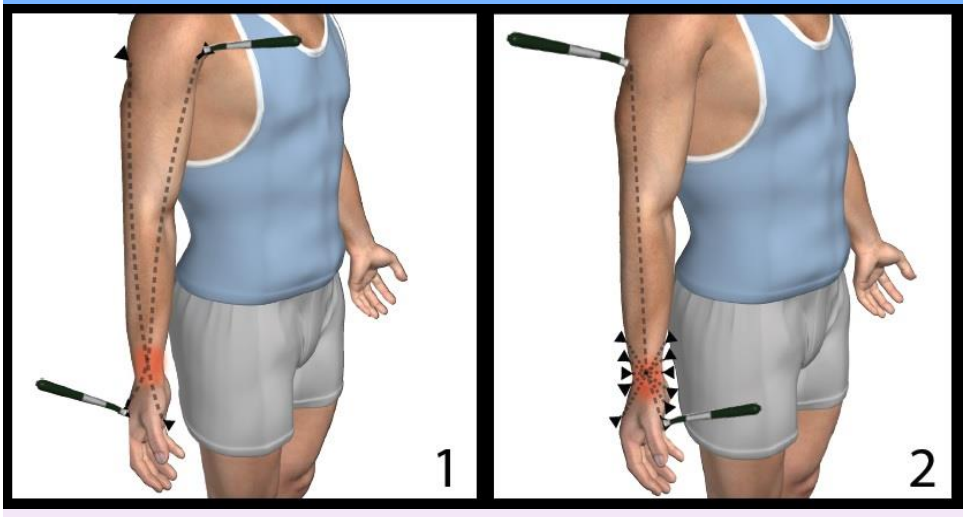
Example 4: Elbow Pain



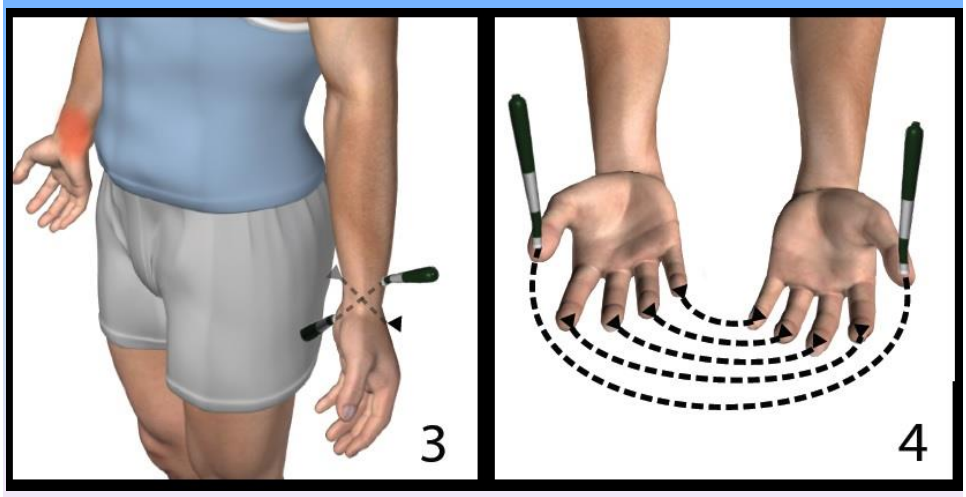
Example 4: Elbow Pain



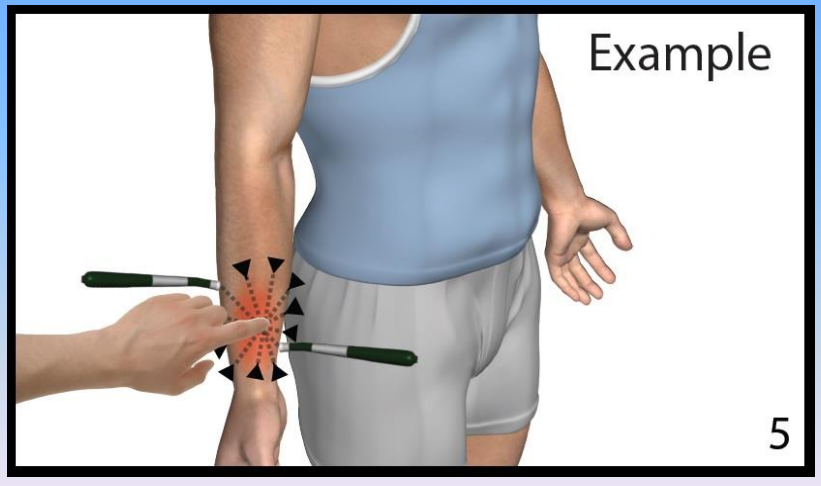
Example 5: Wrist Pain

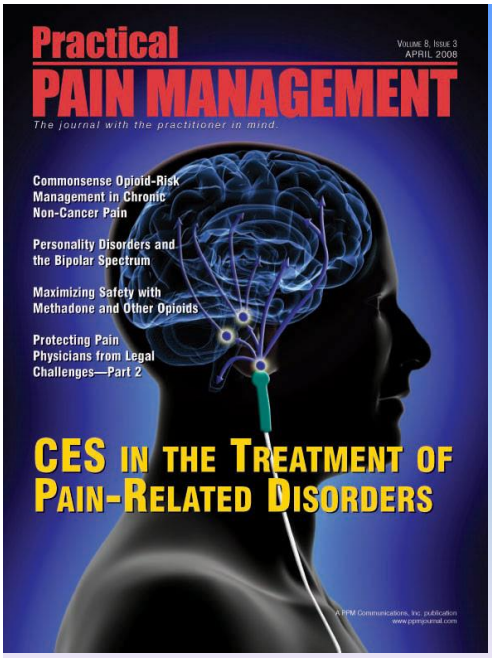


Example 5: Wrist Pain



Example 5: Wrist Pain





Kirsch, Daniel L. and Gilula, Marshall F. CES in the treatment of pain-related disorders.
Practical Pain Management, 8(3):12-25, 2008

Don't Forget About the Brain

Always finish with at least 20 minutes of Alpha-Stim CES

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