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 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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>80%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>80%</td>
</tr>
<tr>
<td>Depression</td>
<td>80%</td>
</tr>
<tr>
<td>Pain</td>
<td>80%</td>
</tr>
<tr>
<td>Headache</td>
<td>80%</td>
</tr>
</tbody>
</table>

Traditional View of Synaptic Activity

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


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).


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.

<table>
<thead>
<tr>
<th>Alert</th>
<th>No “brainfog.” Vision is clear, and energetic as if the patient slept all night</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake</td>
<td>Some patients feel light right away</td>
</tr>
<tr>
<td>Sleepy</td>
<td>HEAVY, GROGGY, EUPHORIC (never stop here)</td>
</tr>
</tbody>
</table>

20 minutes to 1 or more hours

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 horns 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-pons nucleus of the brainstem
NE     norepinephrine
LC     locus ceruleus
5-HT   serotonin


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 (%)
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


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.

Mean Anxiety Scores


Anxiety Improvement in Advanced Cancer Patients

Anxiety improvement in advanced cancer patients, showing significant reduction over weeks of treatment.

PTSD in a 54 Year Old Male Veteran
Overall Decrease in Severity by 39% in One Month

<table>
<thead>
<tr>
<th>PTSD Symptoms Scale – Interview (PSS-I)</th>
<th>PRE</th>
<th>POST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-experiencing (0-15)</td>
<td>34</td>
<td>13</td>
</tr>
<tr>
<td>Avoidance (0-21)</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Increased Arousal (0-15)</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

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


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

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

### Depression Improvement in Advanced Cancer Patients

<table>
<thead>
<tr>
<th></th>
<th>Mean depressive scores in advanced cancer patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital Anxiety and Depression Scale</td>
</tr>
<tr>
<td></td>
<td>N=33</td>
</tr>
<tr>
<td></td>
<td>p=0.024</td>
</tr>
<tr>
<td>Baseline</td>
<td>6.36</td>
</tr>
<tr>
<td>Week 1</td>
<td>5.67</td>
</tr>
<tr>
<td>Week 2</td>
<td>5.27</td>
</tr>
<tr>
<td>Week 3</td>
<td>4.97</td>
</tr>
<tr>
<td>Week 4</td>
<td>5.34</td>
</tr>
</tbody>
</table>


6.36 5.67 5.27 4.97 5.34

### 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.
What is the first thing you think of when your computer breaks?

What is the first thing you think of treating when you have pain?

Pain Reduction in Advanced Cancer Patients

Mean pain scores in advanced cancer patients

Brief Pain Inventory
N=33
p<0.013

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


Percent Improvement in 32 Veterans Across 158 Treatment Sessions


Cumulative Improvement in Pain After 1-5 CES


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

After 1 Month

After 2 Months

After 3 Months

Accumulated Percent Improvement

Time After Treatment Began


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


Alpha-Stim with Medication

Anxiety Scores with Meds Alone vs. Meds Combines with CES

The treatment group had significant reduction in anxiety (31%, P=0.05) over 6 weeks but the CES + med group did significantly better than mediation alone (97%, P=0.01).
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 right now?
✓ 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 2: Back Pain

Example 4: Elbow Pain
Example 5: Wrist Pain


Don’t Forget About the Brain
Always finish with at least 20 minutes of Alpha-Stim CES

Questions? Call 1-800-FOR-PAIN
Email Dr. Jeff Marksberry: jeff@epii.com
www.alpha-stim.com