CRANIAL ELECTROTHERAPY STIMULATION (CES) and the treatment of Depression, Anxiety & Insomnia

Charles A. Fisher
President, Fisher Wallace Laboratories
Humble Beginnings of CES

- 46 AD – Scribonius Largus
  - Black Torpedo Fish

- 1700’s – Charles Kite
  - Electric Defibrillator

- 1850’s – Strange Contraptions
Early Devices

* Electro-medical apparatus, A. Gaiffe, Paris 1868
CES Today

- FDA-Cleared since 1976 for depression, anxiety & insomnia
- Track record of safety
- Scores of published studies, particularly in substance abuse arena
- Portable & battery powered
- Easy-to-Use
- Three key frequencies
Mechanism of Action

- Increases Serotonin*
- Increases Beta-Endorphins*
- Increases GABA*
- Decreases Cortisol*
- Decreases in Neuronal Activity

Unlike tDCS, CES does not polarize the brain. The effects of cranial AC stimulation have been shown to decrease neuronal activity, which may explain reduction in anxiety.

* Proven in blood, cerebral spinal fluid & saliva tests published in peer reviewed journals
Ease of Use

- 20 minutes Treatment Session
  - Shuts Off Automatically
  - One Moving Part
- 30-45 Ideal Treatment Period
- Use with or without medication
- Out-patient, in-patient & home-care
- Low cost and few replaceables
Very Low Risk

- Decades of clinical use and many published studies without adverse events
- No serious side effects
- No contraindications with medication
- Stimulation is far below seizure threshold
- 100X less amperage than TMS and 1000X less than ECT
- Battery powered – Two AA
- AC current = no electrode burns (v. tDCS)
Effectiveness

- Research averages 65% - 70%
- Often eliminates insomnia in first week of use
- Often reduces depression and anxiety within two weeks of use
- May be used in conjunction with medication to lower dosage and thus lower medication side effects
PTSD

“The Cranial Electrotherapy Stimulator (CES) ... stimulates the parasympathetic part of the nervous system which counteracts the stress response, thus reducing the physical symptoms of PTSD such as rapid pulse, shaking, sweating, or a knot in the stomach. It also addresses psychological symptoms by reducing anxiety, restlessness, agitation, anger, depression, and sleep problems. Furthermore, the improvements in emotion regulation reduce the risk of inappropriate impulsive, aggressive behaviors.”

- Richard Brown, MD
  Associate Professor in Clinical Psychiatry
  Columbia University College of Physicians and Surgeons
Summary

**PROS:** Human and animal randomized studies show clinically effective and statistically significant reductions (and remission) in insomnia, depression and anxiety symptoms in selected populations following cranial stimulation. Human studies provide evidence that cranial stimulation produces changes in biochemical components in blood and cerebral spinal fluid that may be associated with the clinical changes found in the randomized studies. No reports of adverse events.

**CONS:** Many studies are older, of small subject size (but still statistically significant), varying patient populations, and employ different CES dosing.
Addiction Recovery Pilot Program

- Largest non-profit drug rehab center in USA
- 392 Subjects – cocaine and heroine addicts
  - 293 Non-CES (control)
  - 99 CES (for first 10 days of detox)
- PTSD & detox symptoms: depression, anxiety, insomnia
Phoenix House – Outcome

• 50% increase in retention after 90 days (versus control group)

• Reported profound reduction of PTSD & detox symptoms (anxiety & insomnia)
Table 2. Comparison of attrition rates between clients who received CES and clients who did not receive CES.

<table>
<thead>
<tr>
<th>Residential treatment attrition</th>
<th>no CES</th>
<th>received CES</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 293</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>at day 7</td>
<td>29 (9.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>at day 14</td>
<td>62 (21.2)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>at day 30</td>
<td>89 (30.4)</td>
<td>10 (10.1)</td>
</tr>
<tr>
<td>at day 60</td>
<td>120 (41.0)</td>
<td>17 (17.2)</td>
</tr>
<tr>
<td>at day 90 *</td>
<td>131 (48.3)</td>
<td>23 (24.0)</td>
</tr>
</tbody>
</table>

*Note: Sample sizes were n=271 and n=96 for the no-CES and CES groups respectively. Excluded from 90 day attrition analyses are 8 clients who completed residential treatment between 60 and 90 days, and 17 clients admitted at the end of May 2009 who have not reached the 90 day timepoint.
Fig. 1. Cox regression model (unadjusted) showing treatment retention for clients who participated in CES and clients who did not.
## Patient Feedback

<table>
<thead>
<tr>
<th>Client Name</th>
<th># of Sessions</th>
<th>Client Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deborah G.</td>
<td>8</td>
<td>Client reports improved concentration, sleeping better</td>
</tr>
<tr>
<td>Timothy C.</td>
<td>4</td>
<td>Client reports he starts his day over with the session, it relaxes him</td>
</tr>
<tr>
<td>Sara R.</td>
<td>5</td>
<td>Client reports feeling a little less stressed</td>
</tr>
<tr>
<td>Maria V.</td>
<td>5</td>
<td>Client reports feeling more relaxed, sleeping better, and less anxious</td>
</tr>
<tr>
<td>Jose V.</td>
<td>6</td>
<td>Client reports feeling more relaxed, and less stress</td>
</tr>
<tr>
<td>Patricia W.</td>
<td>3</td>
<td>Client reports Dot having feeling any different</td>
</tr>
<tr>
<td>Eddar R.</td>
<td>3</td>
<td>Client reports less stressed, relaxed</td>
</tr>
<tr>
<td>Karsheam P.</td>
<td>4</td>
<td>Client reports sleeping better, attitude improvement</td>
</tr>
<tr>
<td>Jason M.</td>
<td>3</td>
<td>Client reports getting better sleep</td>
</tr>
<tr>
<td>Jaclyn T.</td>
<td>2</td>
<td>Client reports sleeping better and feeling better</td>
</tr>
<tr>
<td>Jon T.</td>
<td>2</td>
<td>Client reports sleeping better</td>
</tr>
<tr>
<td>Jason L.</td>
<td>3</td>
<td>Client reports being able to sleep better, and more focused</td>
</tr>
<tr>
<td>Davon H.</td>
<td>2</td>
<td>Client reports feeling more relaxed</td>
</tr>
<tr>
<td>Orlando M.</td>
<td>1</td>
<td>Client reports that he liked the session and wants to continue</td>
</tr>
</tbody>
</table>
Cortical Stimulation

Rescuing cocaine-induced prefrontal cortex hypoactivity prevents compulsive cocaine seeking


Nature 496, 359–362 (18 April 2013) doi:10.1038/nature12024
Received 01 March 2012 | Accepted 18 February 2013 | Published online 03 April 2013

Loss of control over harmful drug seeking is one of the most intractable aspects of addiction, as human substance abusers continue to pursue drugs despite incurring significant negative consequences\textsuperscript{1}. Human studies have suggested that deficits in prefrontal cortical function and consequential loss of inhibitory control\textsuperscript{2,3,4} could be crucial in promoting compulsive drug use. However, it remains unknown whether chronic drug use compromises cortical activity and, equally important, whether this deficit promotes compulsive cocaine seeking. Here we use a rat model of compulsive drug seeking\textsuperscript{2,5,6} in which cocaine seeking persists in a subgroup of rats despite delivery of noxious foot shocks. We show that prolonged cocaine self-administration decreases ex vivo intrinsic excitability of deep-layer pyramidal neurons in the prelimbic cortex, which was significantly more pronounced in compulsive drug-seeking animals. Furthermore, compensating for hypoactive prelimbic cortex neurons with \textit{in vivo} optogenetic prelimbic cortex stimulation significantly prevented compulsive cocaine seeking, whereas optogenetic prelimbic cortex inhibition significantly increased compulsive cocaine seeking. Our results show a marked reduction in prelimbic cortex excitability in compulsive cocaine-seeking rats, and that \textit{in vivo} optogenetic prelimbic cortex stimulation decreased compulsive drug-seeking behaviours. Thus, targeted stimulation of the prefrontal cortex could serve as a promising therapy for treating compulsive drug use.
ADD/ADHD Studies


- Richard Brown, Non-Drug Treatments for ADD/ADHD, New Options for Kids, Adults & Clinicians, 2012

- Cranial Electrotherapy Stimulation, A Monograph, Raymond B. Smith, Ph.D.
Bipolar Depression

A Single Blind, Randomized, Sham Controlled Study of Cranial Electrical Stimulation in Bipolar II Disorder
SS Koppolu, G Kazarians, M Varvara, D McClure, Z Yaseen, AMR Lee, I Galynder
Beth Israel Medical Center, New York, NY

Abstract

Introduction: Cranial Electrical Stimulation (CES) is a non-invasive brain stimulation technology which has been FDA cleared for the treatment of depression, anxiety and insomnia. However, there have not been any clinical trials evaluating its efficacy in treating the depressive phase of bipolar II disorder. This single-blind, randomized, sham-controlled study examined the safety and efficacy of this particular group of patients. Preliminary results of this study are discussed.

Methods: Eight patients with bipolar II disorder currently experiencing depressive symptoms were enrolled in the Hamilton Depression Rating Scale (HDRS) and Hamilton Depression Inventory (HDI) and the quality of life was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q). The assessments were completed at study entry, at the end of the 2nd week (after active treatment in active treatment group) and at the end of the 8th week (after active treatment in sham treatment group). At the end of the 8th week, patients in the active treatment group received open-label active treatment for 2 weeks.

Results: Following this, both groups received open-label active treatment for an additional 2 weeks (plus 2). Depression symptoms were rated using the Hamilton Depression Rating Scale (HDRS), the Back Depression Inventory (BDI), and the quality of life was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q). The assessment was completed at study entry, at the end of the 2nd week (after active treatment in the active treatment group) and at the end of the 8th week (after open-label active treatment) for both groups.

Discussion: CES therapy had a positive treatment effect reducing the level of depression in the experimental group that increased to mild in the control group, and the self-report scale after the period of sham treatment. After an additional two weeks of open-label active treatment the control group also had a slight reduction in depression symptoms levels and marked increase in the level of life satisfaction.

The research was funded by the Rockefeller University.

Demographic characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Active treatment group</th>
<th>Sham control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50 (15-80)</td>
<td>50 (15-80)</td>
</tr>
<tr>
<td>Years of Education</td>
<td>15 (6-30)</td>
<td>15 (6-30)</td>
</tr>
<tr>
<td>Sex</td>
<td>3 (M)</td>
<td>2 (M)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>White</td>
</tr>
<tr>
<td></td>
<td>3 (75%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td></td>
<td>1 (25%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td>1 (25%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

The groups were statistically different on the level of quality of life after the randomized treatment period (p=0.03). CES therapy had a positive treatment effect reducing the level of depression in the experimental group that increased to mild in the control group, and the self-report scale after the period of sham treatment. After an additional two weeks of open-label active treatment the control group also had a slight reduction in depression symptoms levels and marked increase in the level of life satisfaction.

Discussion

The groups were statistically different on the level of quality of life after the randomized treatment period (p=0.03). CES therapy had a positive treatment effect reducing the level of depression in the experimental group that increased to mild in the control group, and the self-report scale after the period of sham treatment. After an additional two weeks of open-label active treatment the control group also had a slight reduction in depression symptoms levels and marked increase in the level of life satisfaction.

References


Ongoing Research

McLean Hospital (Harvard) – PTSD

MGH – Major Depressive Disorder

Beth Israel Medical Center – Bipolar Disorder

NYU / University of Chicago – TBI
Additional Information

www.FisherWallace.com

Chip Fisher, President

chip@fisherwallace.com