Cranial Electrotherapy Stimulation for Treatment of Anxiety, Depression, and Insomnia

Daniel L. Kirsch, PhD[a,*], Francine Nichols, RN, PhD[b]

KEYWORDS

• Cranial electrotherapy stimulation • CES • Anxiety • Depression • Insomnia

KEY POINTS

- Cranial electrotherapy stimulation (CES) is a US Food and Drug Administration–approved, prescriptive, noninvasive electromedical treatment that has been shown to decrease anxiety, insomnia, and depression significantly.
- Side effects from CES are mild and self-limiting (<1%); these include vertigo, skin irritation at electrode sites, and headaches.
- A functional magnetic resonance imaging study showed that CES causes cortical deactivation, producing changes similar to those produced by anxiolytic medications. Electroencephalographic studies show that CES increases alpha activity (increased relaxation), decreases delta activity (reduced fatigue), and decreased beta activity (decreased ruminative thoughts).
- Neurotransmitter studies revealed that CES increased blood plasma levels of β endorphin, adrenocorticotrophic hormone, serotonin, melatonin, norepinephrine, and cholinesterase. CES also decreased serum cortisol levels.
- CES treatments are cumulative; however, most patients show at least some improvement after the first treatment. Depression can take up to 3 weeks for initial response. Insomnia varies widely with some individuals having improved sleep immediately and others not having improved sleep until 2 months into treatment.
- A trial treatment in the office or clinic can identify those individuals who readily respond to CES treatment. CES can also be used during psychotherapy sessions and with medications, hypnosis, and biofeedback to decrease patient anxiety.
- CES is cost-effective compared with drugs and other devices used in psychiatry. It is easy to use in both clinical and home settings.

Conflict of Interest: D.K. is Chairman of Electromedical Products International, Inc; F.N. is Research Consultant for Electromedical Products International, Inc.

[a] The American Institute of Stress, 9112 Camp Bowie West Boulevard #228, Fort Worth, TX 76116, USA; [b] Georgetown University, Washington, DC, USA
* Corresponding author. 2201 Garrett Morris Parkway, Mineral Wells, TX 76067.
E-mail address: dkirsch@stress.org

Psychiatr Clin N Am 36 (2013) 169–176
http://dx.doi.org/10.1016/j.psc.2013.01.006 **psych.theclinics.com**
0193-953X/13/$ – see front matter

INTRODUCTION

Cranial electrotherapy stimulation (CES) uses medical devices about the size of a cell phone that send a pulsed, weak electrical current (<4 mA) to the brain via electrodes placed on the ear lobes, maxilla-occipital junction, mastoid processes, or temples. CES was first cleared for interstate marketing and export by the US Food and Drug Administration for the treatment of anxiety, depression, and insomnia in 1979 and its use in clinical practice has steadily increased over time. The primary treatments used today for anxiety, depression, and insomnia are pharmaceuticals and psychotherapy. Both approaches have limitations in terms of effectiveness, side effects, costs, or time required. During the last decade, an increasing number of psychiatrists are integrating CES treatments into their clinical practice because it is noninvasive, has few side effects (1% or less), and treats anxiety, depression, and insomnia simultaneously. However, many clinicians are still unfamiliar with the considerable scientific evidence demonstrating the efficacy of some CES devices. This article summarizes neurophysiologic effects and the clinical research on CES as well as methods for integrating CES into the treatment of anxiety, depression, and insomnia.

NEUROPHYSIOLOGIC EFFECTS AND RESEARCH STUDIES

The brain functions electrochemically and can be readily modulated by electrical intervention. Research conducted at the Biomedical Engineering Program of the University of Texas at Austin indicated that from 1 mA of current, about 5 $\mu A/cm^2$ of CES reaches the thalamic area at a radius of 13.30 mm and may facilitate the release of neurotransmitters, which in turn could cause physiologic effects such as relaxation.[1] CES is believed to affect the subcortical brain structures known to regulate emotions, such as the reticular activating system, thalamus, and hypothalamus, as well as the limbic system. CES may stimulate regions that regulate pain messages, neurotransmitter function, and hormone production via the hypothalamic-pituitary axis.[2] CES treatments induce significant changes in the electroencephalogram, increasing alpha (8–12 Hz) relative power and decreasing relative power in the delta (0–3.5 Hz) and beta (12.5–30 Hz) frequencies.[3] Increased alpha correlates with improved relaxation and increased mental alertness or clarity. Decreased delta waves indicate a reduction in fatigue. Beta-wave reductions between 20 and 30 Hz correlate with decreases in anxiety, ruminative thoughts, and obsessive/compulsive-like behaviors.

Low-resolution electromagnetic tomography and functional magnetic resonance imaging studies showed that CES reached all cortical and subcortical areas of the brain, producing changes similar to those induced by anxiolytic medications.[4,5] Many symptoms seen in psychiatric conditions, such as anxiety, insomnia, and attention deficit disorders, are thought to be exacerbated by excess cortical activation.[6,7] A recent functional magnetic resonance imaging study showed that CES causes cortical brain deactivation in the midline frontal and parietal regions of the brain after one 20-minute treatment.[4]

CES treatments have been found to induce changes in neurohormones and neurotransmitters that have been implicated in psychiatric disorders: substantial increases in beta endorphins, adrenocorticotrophic hormone, and serotonin; moderate increases in melatonin and norepinephrine, modest or unquantified increases in cholinesterase, gamma-aminobutyric acid, and dehydroepiandrosterone, and moderate reductions in cortisol.[8,9] **Table 1** shows some of the chemical changes associated with use of the LISS CES device.

Table 1
Mean changes in neurochemicals in blood plasma after one 20-minute CES session

Neurochemical	Change	Implications
Beta endorphin	↑ 98%	Decreases pain
Adrenocorticotrophic hormone	↑ 75%	Promotes homeostasis
Serotonin (5HT)	↑ 50%	Improves mood Increases pain tolerance Decreases insomnia
Melatonin	↑ 25%	Induces sleep
Norepinephrine	↑ 24%	Increases pleasure Increases arousal
Cortisol	↓ 18%	Reduces stress response
Cholinesterase	↑ 8%	Increases relaxation
gamma-Aminobutyric acid	↑[a]	Decreases spasticity
Dehydroepiandrosterone	↑[a]	Improves immune system functioning

[a] Percentage increase not stated in source.

Cranial Electrotherapy Stimulation for Anxiety, Depression, Insomnia

There is a wealth of data on CES from more than 40 years of research. In 3 randomized, double-blind, sham-controlled studies and 1 investigator-blind study with a control group that included 227 subjects, the active CES groups had significantly lower scores on anxiety outcome measures than the sham or control groups.[10–13] Effect sizes ranged from $d = -0.60$ (moderate) to $d = -0.88$ (high). Effect sizes from 2 open clinical trials (N = 208) investigating the efficacy of CES for anxiety were also robust at $d = -0.75$ (moderate) and $d = -1.52$ (very high) on the Four-dimensional Anxiety and Depression Scale and the Hamilton Anxiety Rating Scale (HARS), respectively.[14,15] CES was also shown to decrease depression[14,16] and insomnia significantly.[17,18] These studies used the Alpha-Stim (Electromedical Products International, Inc, Mineral Wells, Texas) brand of CES device with reliable and valid outcome measurement scales. A limitation of these CES randomized controlled trials (RCT) is that they were small with the number of subjects ranging from 33 to 74. These studies need to be replicated with a larger number of subjects. Three studies[11–13] used a rigorous double-blind, sham-controlled RCT design, whereas the remaining studies cited were RCTs or open-label studies. Additional, ongoing double-blind, sham-controlled RCTs with larger numbers of subjects, funded by the National Institutes of Health, Department of Defense, and Veterans Administration, will strengthen the evidence for CES treatments.

Cranial Electrotherapy Stimulation for Assaultive Behavior

Preliminary research on the use of CES in psychiatric populations is extending to assaultive behaviors. Forty-eight chronically aggressive neuropsychiatric patients were treated for at least 2 to 3 months with CES at North Texas State Hospital at Vernon, a maximum security psychiatric hospital.[19]

- The patients, ages 18 to 62, had been hospitalized from a few months to more than 20 years and included many of the most resistant patients in the maximum security unit.
- The patients remained on their antipsychotic and mood stabilizing medications during CES.

- Every patient had multiple comorbidities: 45 of the 48 carried psychotic diagnoses; mental retardation was present in 31, and central nervous system trauma was etiologic in 6. Well-controlled seizure disorders were noted in 18.
- Some form of personality disorder was diagnosed in almost all cases, but only 3 were diagnosed primarily with antisocial personality disorder.
- Two patients had Huntington chorea, and 2 others had pervasive developmental disorder with psychosis.
- One patient met criteria for intermittent explosive disorder.
- Psychotic diagnoses included schizoaffective disorder, 12 (all manic); disorganized schizophrenia, 8; paranoid schizophrenia, 7; undifferentiated schizophrenia, 5; and bipolar disorder (manic), 2.
- Of the 48, 41 had been declared manifestly dangerous.
- The remaining 7 patients had been found incompetent to stand trial on felony charges involving bodily injury.

Forty of the 48 (83%) responded positively to CES. In the 3 months before CES, the group committed 1301 acts of aggression. During the 3 months of active CES treatment, there were 767 acts of aggression, a decline of 41% ($P<.001$). Seclusions declined 40% ($P = .05$) from 199 to 120, and the number of times patients required restraint decreased 40% ($P<.001$) from 446 to 268. Frequency of PRN medication declined 42% ($P<.01$) from 648 times over 3 months pretreatment to 377 times during 3 months of active treatment. The decrease of 271 PRN medication doses in 3 months resulted in a savings of more than $12,000 for these medication expenses alone. Overall, 32 of the 48 patients were able to be discharged from the hospital, and none returned for at least 2 years, as of the presentation by Childs at the American Psychiatric Association annual conference in 2007. Five of the 6 central nervous system trauma cases improved. Among the 7 patients previously incompetent to stand trial, 6 who responded to CES were subsequently found competent and have been returned to the courts for judicial processing. Two other patients, one of whom was primarily antisocial, and the other with pronounced antisocial traits, were nonresponders to CES.

CLINICAL CONSIDERATIONS AND GUIDELINES

To integrate CES into the practice of psychiatry for the treatment of anxiety, posttraumatic stress disorder, depression, and insomnia, the authors recommend a trial series of treatments in a clinic or office to evaluate responses in each individual. After the initial trial, patients can be prescribed a CES device to use at home, giving them increased control over the management of their symptoms. In addition to a regular 20- to 60-minute treatment daily or every other day, patients can add treatments as needed. Some clinicians find it useful to set up a CES lounge where patients can come in for treatments whenever they feel stressed.

Cranial Electrotherapy Stimulation During Psychotherapy Sessions

CES may also be used during psychotherapy sessions. Using CES during a therapy session decreases anxiety and usually improves the patient's ability to share problems, concerns, and worries with the therapist, as well as to respond to the therapist's questions more effectively. Anecdotal reports from psychiatrists and other mental health professionals on the use of CES during therapy are consistently enthusiastic. CES induces a prehypnotic relaxed state of mind and body that is complementary with many other interventions.

Concurrent Pharmacotherapy

CES can be used with pharmacologic therapy without concern about potential medication interactions. However, it is important to inform the patient that CES may decrease the need for medication. As the patient improves, both the psychiatrist and the patient should be alert for symptoms that may indicate a need for a dosage adjustment.[20]

Self-directed Home Treatment

Most individuals are capable of doing self-directed CES therapy at home. Treatments may need to be performed daily during the first 1 to 3 or 4 weeks and then 2 to 3 times per week during a maintenance phase. The individual can also use CES as often as needed, as there are no side effects from extended use, which is especially beneficial for those individuals diagnosed with posttraumatic stress disorder and those who experience panic attacks.

EVALUATING IMMEDIATE AND LONG-TERM EFFECTS

Feelings experienced during a CES treatment are shown in **Fig. 1**. If the patient feels heavy, groggy, or euphoric at the end of the allotted time, it is important to continue the treatment session until the patient feels "light." At the end of a CES session, most patients will feel more relaxed, yet alert, and have an increased sense of well-being.

Evaluating a single 20- to 40-minute trial of CES in a clinic or office will help identify those individuals who most readily respond to CES. However, CES effects are cumulative so those who do not respond initially may benefit when given daily treatments (20–60 minutes) for 1 month or longer.[21]

A psychiatrist who would like to document treatment progress in CES patients may chose to use the HARS, Hamilton Depression Rating Scale 17, and/or the Pittsburgh Sleep Quality Index, all of which have proven useful in evaluating CES outcomes. The

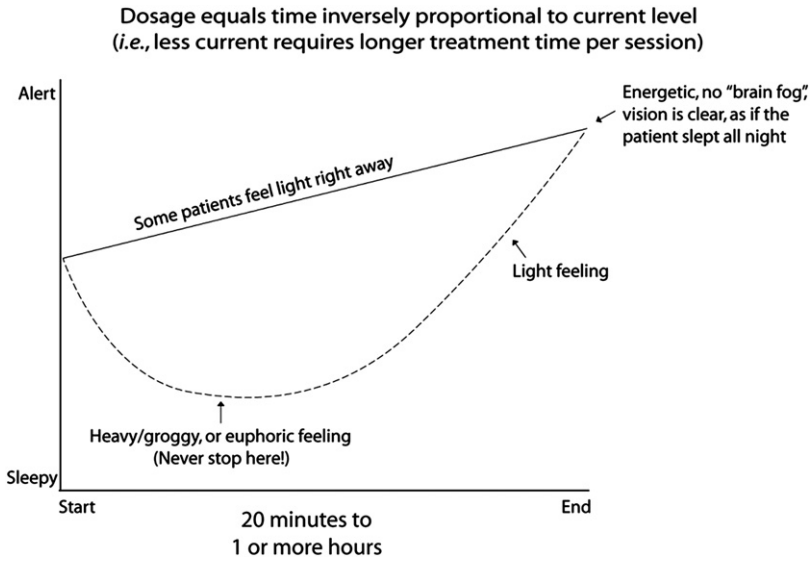

Fig. 1. Feelings experienced during CES treatment stages.

HARS should be administered before and immediately after the first treatment and after 3 weeks and 6 weeks of daily use. For depression and insomnia, which typically respond more slowly, patients should be tested before, but not immediately after, the first treatment. Measurements at 3 weeks and 6 weeks provide useful assessments of patient progress.

CONTRAINDICATIONS, PRECAUTIONS, AND ADVERSE EFFECTS OF CRANIAL ELECTROTHERAPY STIMULATION

There are no known contraindications to the use of CES. The only precaution is regarding use during pregnancy. A study of potential teratogenic effects from CES was conducted on 844 Spraque-Dawley fetal rats.[22] The treated rats were divided into 3 groups and given CES 1 hour daily throughout their pregnancy at either 10, 100, or 1000 Hz, while the parameters of 1 V, 0.125 mA, at a 0.22-microseconds pulse width remained constant. On day 18 of pregnancy, the dams were killed and cesarean section was performed immediately. After thorough external examination, autopsies evaluated the palate, heart, major vessels, lungs, liver, kidneys, ureters, and bladder. Examinations under light microscopy revealed no neural tube defects, limb reduction deformities, or anterior abdominal wall abnormalities in the controls or in any of the treatment groups. Skeletal surveys of the fetal rats found no vertebral column, rib, or long bone deformities. Comparison between groups revealed more pregnancy resorptions and fewer offspring in all treatment groups compared with the control group, with the difference only reaching significance in the 1000-Hz treatment group. Average fetal weights were inversely proportional to frequency and were significantly different among groups. Fetal brain weight followed a similar pattern of reduction, except that weights were not significantly different between the medium and highest frequency treatment groups.

In their discussion, the researchers stated that, whereas the incidence of congenital anomalies was zero, the reason pregnancy resorptions were increased may be due to the CES-treated rats being more complacent. Their behavior resembled the calming effects of CES in humans. The treated rats were not as active as the control rats. Accordingly, it is possible that food intake was lowered in the treatment group, a reasonable implication given the reduction in fetal weights. They concluded that CES may be embryolethal in the very early stages of pregnancy in the rat and might cause some miscarriages, especially at 1000 Hz, but there is no evidence of fetotoxic effects. The relevance of these findings to humans is unknown.

Adverse effects of CES in humans occur in less than 1% of cases and they are usually mild and self-limiting. These adverse effects include vertigo, skin irritation at electrode sites, and headaches. Headaches and vertigo are usually associated with the current being set too high for the individual. These effects resolve when the current is reduced or within minutes to hours following treatment. Irritation at the electrode site can be avoided by moving electrodes around slightly during treatments. No serious adverse effect has ever been reported from using CES.[23]

SUMMARY

CES can improve the safety and efficacy of treatment of anxiety, insomnia, and depression. When prescribed for home use, patients are empowered to regulate their own moods and to overcome their sleep problems, thus enhancing patient outcomes. Compared with other neuerostimulation techniques for brain repair, CES is noninvasive and less expensive and can be used safely and conveniently by patients at home. It is useful as an adjunct to medication or psychotherapy or as a stand-alone treatment. Historically CES has been used as a last resort when medications and other

interventions fail or are not well tolerated. With an increase in the evidence base for positive outcomes, more physicians are recognizing CES as a first-line or adjunctive treatment.

REFERENCES

1. Ferdjallah M, Bostick FX, Barr RE. Potential and current density distributions of cranial electrotherapy stimulation (CES) in a four concentric-spheres model. IEEE Trans Biomed Eng 1996;43:939–43.
2. Kirsch DL. Cranial electrotherapy stimulation for the treatment of anxiety, depression, insomnia and other conditions. Insert: Giordano, James. Illustrating how CES works. Nat Med 2006;23:118–20.
3. Kennerly R. QEEG analysis of cranial electrotherapy: a pilot study. J Neurother 2004;8:112–3.
4. Feusner JD, Madsen S, Moody TD, et al. Effects of cranial electrotherapy stimulation on resting state brain activity. Brain Behav 2012;2(3):211–20.
5. Kennerly RC. Changes in quantitative EEG and low resolution tomography following cranial electrotherapy stimulation. Ph.D. Dissertation, the University of North Texas. 529 pp, 81 tables, 233 figures, 171 references, 2006.
6. Yassa MA, Hazlett RL, Stark CE, et al. Functional MRI of the amygdala and bed nucleus of the stria terminalis during conditions of uncertainty in generalized anxiety disorder. J Psychiatr Res 2012;46:1045–52.
7. Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. Sleep Med Rev 2010;14:9–15.
8. Shealy CN, Cady RK, Culver-Veehoff D, et al. Cerebrospinal fluid and plasma neurochemicals: response to cranial electrical stimulation. J Neuro Orthop Med Surg 1998;18:94–7.
9. Liss S, Liss B. Physiological and therapeutic effects of high frequency electrical pulses. Integr Physiol Behav Sci 1996;31:88–96.
10. Kim HJ, Kim WY, Lee YS, et al. The effect of cranial electrotherapy stimulation on preoperative anxiety and hemodynamic responses. Korean J Anesthesiol 2008; 55:657–61.
11. Cork RC, Wood PM, Norbert C, et al. The effect of cranial electrotherapy stimulation (CES) on pain associated with fibromyalgia. Internet J Anesthesiol 2004;8:1–7.
12. Lichtbroun AS. The treatment of fibromyalgia with cranial electrotherapy stimulation. J Clin Rheumatol 2001;7:72–8.
13. Winick RL. Cranial electrotherapy stimulation (CES): a safe and effective low cost means of anxiety control in a dental practice. Gen Dent 1999;47:50–5.
14. Bystritsky A, Kerwin L, Feusner JD. A pilot study of cranial electrotherapy stimulation for generalized anxiety disorder. J Clin Psychiatry 2008;69:412–7.
15. Overcash SJ. Cranial electrotherapy stimulation in patients suffering from acute anxiety disorders. American J Electromed 1999;16:49–51.
16. Kirsch DL, Gilula M. Cranial electrotherapy stimulation in the treatment of depression – part 2. Pract Pain Manag 2007;7:32–40.
17. Taylor AG, Anderson JG, Riedel SL, et al. Cranial electrical stimulation improves symptoms and functional status in individuals with fibromyalgia. Pain Manag Nurs, in press.
18. Kirsch DL, Gilula MF. CES in the treatment of insomnia: a review and meta-analysis. Pract Pain Manag 2007;7:30–43.

19. Childs A, Price L. Cranial electrotherapy stimulation reduces aggression in violent neuropsychiatric patients. Prim Psychiatr 2007;14:50–6.
20. Stanley TH, Cazalaa JA. Transcutaneous cranial electrical stimulation decreases narcotic requirements during neurolept anesthesia and operation in man. Anesth Analg 1982;61:863–6.
21. Holubec JT. Cumulative response from cranial electrotherapy stimulation (CES) for chronic pain. Pract Pain Manag 2009;9:80–3.
22. Little B, Patterson MA. Embryofetal effects of neuroelectric therapy (NET). Electromagnetic Biology and Medicine 1996;15(1):1–8.
23. Electromedical Products International, Inc, CES safety data submitted to FDA, February 10, 2012. Available at: http://www.alpha-stim.com/wp-content/uploads/EPIs-fda-presentation.pdf. Accessed November 2, 2012.