



Cranial Electrotherapy Stimulation for the Treatment of Depression

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ABSTRACT

More prevalent in women than men, clinical depression affects approximately 15 million American adults in a given year. Psychopharmaceutical therapy accompanied by psychotherapy and wellness interventions (e.g., nutrition, exercise, counseling) is effective in 80% of diagnosed cases. A lesser known adjunctive therapy is that of cranial electrotherapy stimulation (CES). The major hypothesis for the use of CES in depression is that it may reset the brain to pre-stress homeostasis levels. It is conjectured that the pulsed

electrical currents emitted by cranial electrical stimulators affect changes in the limbic system, the reticular activating system, and/or the hypothalamus that result in neurotransmitter secretion and downstream hormone production. While evidence is good for applied research, basic research about the mechanisms of action for CES remains in its infancy. A review of the literature provides an overview of current research findings and implications for clinical mental health practice.

Clinical depression, more prevalent in women than men, affects approximately 15 million American adults in a given year, earning the title of the “common cold” of mental health (National Institute of Mental Health [NIMH], 2010). It is estimated that by 2020, depression will be the second most prevalent health problem in the world (World Health Organization [WHO], 2010). Defined as “a mood disorder in which feelings of sadness, loss, anger, or frustration interfere with everyday life for an extended period of time” (Medline Plus, 2009), clinical depression can be debilitating. Frequently accompanying addiction and anxiety disorders, as well as most chronic illnesses, depression affects an individual’s physical and psychological health and interferes with interpersonal relationships. Psychopharmaceutical therapy accompanied by psychotherapy and wellness interventions such as nutrition, exercise, and counseling is effective in 80% of diagnosed cases (Medline Plus, 2009). A lesser known adjunctive therapy is cranial electrotherapy stimulation (CES).

CES delivers pulsed electrical microcurrents transcutaneously (noninvasive) to induce an alpha state of relaxation. Most portable CES devices are small (4 to 5 inches by 2.5 to 3 inches by 1 to 2 inches) and lightweight (3.5 to 5.5 ounces), with currents generated by a 9-volt battery and delivered via ear-clip electrodes. The currents are limited to 600 microamperes (μA)—far less wattage than that required to power a light bulb—and move electrons through the brain at a variety of frequencies known as “harmon-

ic resonance” (Kirsch & Gilula, 2007a). During treatment, an electroencephalogram (EEG) demonstrates normalization of brain electrical patterns. While physically unaware of the current, most people describe feeling more alert, focused, and relaxed following treatment.

HISTORICAL BACKGROUND OF CES

Toward the end of the 18th century, a medical correspondent reported to Benjamin Franklin that following an accidental electric shock to his head, he found his “judgment infinitely more acute...a liveliness in my whole frame” (Bajbouj & Heuser, 2009, p. 1). Although attempts to interest physicians were unsuccessful at that time, electrical brain stimulation re-emerged at the beginning of the 20th century in France (Kirsch, 2002). When the electroconvulsive therapy (ECT) of the late 1930s caused loss of consciousness rather than sleep, scientists began experimenting with lower levels of electrical current, producing what became known as *electroanesthesia* and eventually, *electrosleep* (Gilula & Kirsch, 2005).

Research findings from early studies conducted in Russia during the 1950s began appearing in the literature in the 1960s, with appropriate devices available to clinical investigators in the 1970s (Shealy & Thomson, 2008), the same time psychopharmaceuticals began to emerge (Gilula & Kirsch, 2005). When the U.S. Food and Drug Administration (FDA) was given control over medical devices in 1976, the misnomer *electrosleep* was changed to *cranial electrotherapy stimulation* and the procedure was subsequently approved for treatment

of anxiety, depression, and insomnia (Kirsch, 2006).

PATHOPHYSIOLOGY OF DEPRESSION

The two prevailing hypotheses about the etiology of major depressive disorder (clinical depression) are the monoamine hypotheses: (a) a deficiency of the catecholamines (norepinephrine, epinephrine, and dopamine) causes depression, and (b) a deficiency of serotonin causes depression (Cowen & Harmer, 2009). Research has demonstrated that depression follows a deficit of brain monoamines, norepinephrine, epinephrine, dopamine, and serotonin—all of which serve as neurotransmitters—and, further, that exposure to environmental stressors disrupts the synthesis and utilization of norepinephrine, changes dopamine activity, and alters the synthesis of serotonin (Grippio & Johnson, 2009). The fact that the metabolites of these three monoamines (i.e., norepinephrine, dopamine, serotonin) are reduced in the cerebrospinal fluid of depressed individuals provides additional support for the monoamine hypotheses of depression (Takahashi, 2006). Another indication of the veracity of these two hypotheses is that the three main classes of drugs used to treat depression (i.e., monoamine oxidase inhibitors [MAOIs], tricyclic antidepressant agents [TCAs], selective serotonin reuptake inhibitors [SSRIs]) exert their therapeutic effects by raising synaptic levels of these neurotransmitters. MAOIs block metabolism of the monoamines; TCAs inhibit the presynaptic reuptake of the monoamines, noradrenaline, and serotonin; and SSRIs inhibit the reuptake of serotonin. All

three medication classes have the same end result: increased synaptic levels of the monoamine neurotransmitters (Cirauro, Tsirulnik-Barts, Shader, & Greenblatt, 2004; Goldstein & Potter, 2004).

Elevations of the hormones of the hypothalamic-pituitary-adrenal axis (HPAA) are often observed in individuals who are clinically depressed. A major laboratory finding related to the HPAA, discovered almost 40 years ago and supported by later studies, was the association of hypercortisolemia with depression (Asnis, Sachar, Halbreich, Nathan, Novacenko, et al., 1981; Rubin, Poland, Lesser, Martin, et al., 1987; Rubin, Poland, Lesser, Winston, & Blodgett, 1987; Sachar, Hellman, Fukushima, & Gallagher, 1970; Sachar et al., 1973).

The precise physiological mechanisms whereby CES reduces depression remain unknown. The major hypothesis for the use of CES in depression is that it may reset the brain to pre-stress homeostasis levels. It is conjectured that the pulsed electrical currents emitted by cranial electrical stimulators affect changes in the limbic system, the reticular activating system, and/or the hypothalamus that alter neurotransmitter secretion and downstream production of cortisol (Fisher, 2009; Gibson & O'Hair, 1987; Gilula & Kirsch, 2005; Madden & Kirsch, 1987).

Liss and Liss (1996) showed that transcranial electrical stimulation resulted in increased serotonin in plasma and cerebrospinal fluid, decreased plasma tryptophan (a precursor of serotonin), increased plasma and cerebrospinal beta endorphins, and decreased serum cortisol. All of these findings are

consistent with the hypothesis that CES may reset these neurotransmitters and hormones to pre-stress homeostatic levels.

CES RESEARCH

Much of the early CES research revolved around process issues: wave forms, pulse rates, and current intensities. The



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next research questions to be explored were optimal length of treatment and measurement of outcomes using proven instruments. Early studies included patients with depression that was nonresponsive to treatment. While length of CES treatment (30 minutes) was held constant, frequency was increased from three to five times per week before measurable changes in levels of depression were noted. Having determined the most effective dosage and frequency of treatment, researchers turned their attention to outcomes.

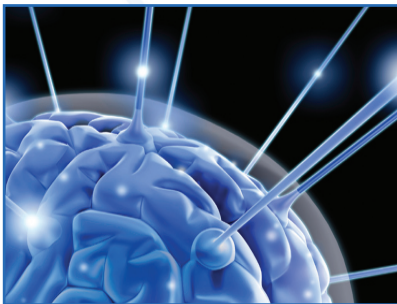
Using established standards, researchers examined the efficacy of CES in treatment of acute and chronic pain, gastrointestinal disorders, neurological insults (e.g., strokes, spinal cord injuries) and malfunctions (e.g., epilepsy), insomnia, and mental health disorders (e.g., anxiety, depression, posttraumatic stress disorder, addiction).

In 2005, Gilula and Kirsch published an extensive review of studies evaluating the effectiveness of CES in various populations. Analysis of longitudinal data (collected from 1 week to 2 years posttreatment) from such studies revealed continued improvement of at least some of the participants in 16 of 17 studies. Another review of 26 published studies specifically examining the use of CES in depression reported positive outcomes in 81% of the investigations (Gilula & Kirsch, 2005). The lack of positive outcomes in the remaining 19% was attributed to the use of older primitive CES devices.

Findings from later studies have supported these analyses. Shealy and Thomlinson (2008) reported a 50% to 60% improvement rate demonstrated by decreasing Zung Depression Scale scores. They further described a higher improvement rate (85%) when CES was combined with nutrition education, vibratory music, and photostimulation. By their account, the significant improvements seen during the first month of treatment persisted for a minimum of 6 months. In fact, they stated, "Some individuals have been followed at our clinic for more than 20 years without recurrence of depression" (Shealy & Thomlinson, 2008, p. 97).

While evidence is good for applied research, basic research

about the mechanisms of action for CES remains in its infancy. Using functional magnetic resonance imaging, Bystritsky et al. (2009) demonstrated that CES current reaches all cortical and subcortical regions of the brain. Researchers have also shown that serotonin and beta-endorphins increased in plasma and cerebrospinal fluid and that cortisol levels decreased in plasma following CES (Liss & Liss, 1996; Shealy, Cady, Culver-Veehoff, Cox, & Liss, 1998; Shealy et al., 1989). Replication of these findings would strengthen the basic science related to the



mechanisms through which CES reduces depression.

Current research complies with double-blinding criteria for clinical trials using sham CES devices with nonconductive wires. To assure that currents are imperceptible to members of the intervention group, currents are curbed at below sensory levels (100 μ A). This lower current setting requires that the treatments be extended in duration (60 minutes). Rose, Taylor, and Bourguignon (2009) conducted a randomized, double-blind, controlled study with care providers of a spouse with Alzheimer's disease. This pilot study involved 38 participants, with equal numbers ($n = 19$) in the treatment and control groups. After completing the Geriatric Depression Scale (GDS), participants were

instructed to wear the device for 1 hour daily during a 4-week period. While the researchers reported no statistically significant differences between groups, both groups reported a decrease in symptoms and postintervention GDS scores.

CLINICAL IMPLICATIONS

CES treatment may be provided at the clinical site or at home using small portable devices. After being moistened with a conducting solution, the electrodes are clipped to the superior aspect of both earlobes as close to the jaw as possible

and increased mental focus, while others experience such deep relaxation that they are advised to avoid driving a car or operating heavy machinery for several hours (Gilula & Kirsch, 2005). CES treatment has no negative side effects beyond the rare occurrence of self-limiting headaches (0.2%), skin irritation (0.11%), or lightheadedness (Kirsch, 2002).

CES for the treatment of depression is prescribed daily for a minimum of 3 weeks, followed by reduced schedule (every other day) or as needed for up to 1 year (Kirsch & Gilula, 2007b).

Whether used alone or in conjunction with pharmaceutical agents, CES has been shown to be an effective and economical therapy for mild to moderate depression.

(Kirsch, 2002). The current is initiated at low levels and gradually increased. If the current is too high, patients may report a stinging pain at the site, dizziness, or nausea. Immediately reducing the current will alleviate these symptoms. Most patients report no sensation at optimal level, but some may experience a tingling sensation at the electrode application site. The current can be adjusted until the patient is comfortable. Many patients are able to continue with routine quiet activities (e.g., reading, using the computer, watching television) during the 20- to 60-minute treatments.

No published research findings have predicted how individuals will react to the treatment. Some patients report immediate reductions in anxi-

No data prohibit the use of CES while taking antidepressant medications. Indeed, it is possible that CES may decrease initial transitory adverse effects of some SSRIs (Gilula & Kirsch, 2005). Drug dosages may need adjustment to lower levels, and using CES in combination with a single pharmaceutical agent may eliminate the need for multiple antidepressant agents, thus reducing the cost of long-term therapy (Kirsch & Gilula, 2007a). Patients do not become dependent on CES, nor does tolerance develop.

Although the FDA does not identify any exclusions to the use of CES, device manufacturers have identified safety issues that require further clinical research. Because the augmentation effects of CES are not

completely known, patients should be advised to avoid concurrent use of botanical agents with known antidepressant properties, such as ginkgo biloba or St. John's wort (Rose et al., 2009). While use of CES is contraindicated in patients with pacemakers or other implanted electronic devices, it has been used safely in patients previously diagnosed with and receiving treatment for epilepsy (Shealy & Thomlinson, 2008). In accordance with FDA regulations, CES device labeling includes precautions regarding use by pregnant women.

Although available for sale over the counter in many countries, CES devices are regulated by the FDA in the United States and require a prescription from a health care provider. The cost of the device varies from company to company, ranging from \$250 to \$1,000. Out-of-pocket costs to the patient will vary with type of insurance coverage. It is estimated that while the initial expense may be greater than that of medication, there is an overall cost savings within the first year of use (Gilula & Kirsch, 2005).

Providers planning to incorporate CES into treatment regimens are advised to attend continuing education sessions offered by the device manufacturers. In addition, all providers are ethically required to educate their patients regarding the therapy, including a risk-benefit analysis. As with any intervention, treatment should be individualized to the specific patient.

SUMMARY

To date, whether used alone or in conjunction with pharmaceutical agents, CES has been shown to be an effective and

KEY POINTS

1. Cranial electrotherapy stimulation (CES) delivers pulsed electrical microcurrents transcutaneously (noninvasive) to induce an alpha state of relaxation by resetting neurotransmitters and hormones to pre-stress homeostatic levels.
2. Using CES in combination with a single pharmaceutical agent may eliminate the need for multiple antidepressant agents, thus reducing the cost of long-term therapy.
3. With few contraindications and few adverse reactions to its use, CES has been shown to be an effective and economical therapy for mild to moderate depression.

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economical therapy for mild to moderate depression. Its use has few contraindications and few adverse reactions. Patients may find this alternative therapy attractive because the treatments can be completed in their own home while continuing with usual activities. In addition, it may provide patients with the feeling that they are actively controlling the disorder, while allowing them to decrease the amount of prescribed medications. As Gilula and Barach (2004, p. 1269) editorialized, "CES is not a miraculous modality, but it's definitely worth a try!"

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