

### **Q. What is Cranial Electrotherapy Stimulation?**

**A.** Cranial electrotherapy stimulation (CES), also known as ‘transcranial electrostimulation,’ ‘electrosleep therapy,’ and ‘electronarcosis,’ is a Food and Drug Administration (FDA)-approved, non-invasive treatment for insomnia, anxiety and depression. CES involves the transcranial application of electrical magnetic fields to the scalp, at levels that do not induce seizure (Rosa & Lisanby, 2012). CES includes a range of techniques, but all methods use low-level alternating electrical signals applied to the scalp or earlobes. In the United States, CES devices require a prescription from a licensed health care practitioner, though the treatment itself is self-administered using hand-held, electrical devices, and there is significant variation in frequency and duration of treatment (Kavirajan et al., 2014).

### **Q. What are the potential mechanisms of action underlying CES?**

**A.** While the mechanism of action of CES is unclear, CES is hypothesized to induct neuroplasticity by repeated electrical stimulation of cortical circuits (Rosa & Lisanby, 2012). Research has shown that weak cranial currents applied during sleep can affect memory; weak electric fields can affect neural function; and, additionally, changes in neurotransmitters and hormones have been found, including increased levels of monoamines in the brain (Rosa & Lisanby, 2012; Kavirajan et al., 2014).

### **Q. Is CES recommended in the Military Health System (MHS)?**

**A. No.** CES is not recommended by the 2016 VA/DoD *Clinical Practice Guideline for the Management of Major Depressive Disorder* for the treatment of major depressive disorder (MDD), and thus has not met the burden of evidence required by the most recent VA/DoD publication.

*The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.*

### **Q. Do other authoritative reviews recommend CES for MDD?**

**A. No.** Other authoritative reviews have not substantiated CES for MDD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) Systematic Review Repository and the Cochrane Database of Systematic Reviews.

- AHRQ: CES was not included in a 2011 comparative effectiveness review (Gaynes et al., 2011) of nonpharmacologic interventions for treatment-resistant depression in adults, though other somatic treatments were included.
- Cochrane: A 2014 systematic review (Kavirajan et al., 2014) found no high quality clinical trials of CES in people with acute depression.

### **Q. Is there any recent research on CES as a treatment for MDD?**

**A.** A January 2017 literature review found two trials published after the 2014 Cochrane systematic review that found no high quality double-blind clinical trials of CES for acute depression. One trial, a double blind pilot study of CES as an add-on intervention for treatment-resistant MDD, compared CES to sham CES (Mischoulon et al., 2014). No significant differences were found between groups on measures of depression symptoms or remission rates. In addition to the limitation of a small sample size (n = 30), the

sham CES condition in this trial did not include a tingling sensation, possibly compromising blinding. As an augmentation trial, results may not provide evidence on the use of CES as a monotherapy. A second study, a double-blind randomized controlled trial (RCT) of CES in primary care patients with anxiety disorders and comorbid depression, found a significant reduction in anxiety and comorbid depression symptoms (Barclay & Barclay, 2014). This trial had a larger sample size, with data analyzed from 108 participants. These results may not be generalizable to patients with depression only. As with the first trial, the sham CES condition in this trial did not include a tingling sensation, possibly compromising blinding.

## **Q. What conclusions can be drawn about the use of CES as a treatment for MDD in the MHS?**

**A.** FDA approval of CES for the treatment of MDD was obtained in 1979, before the requirement for submission of clinical trial data on safety and efficacy. Since then, new CES devices have been cleared for marketing without submission of this data due to an FDA provision permitting that new devices be granted marketing approval if deemed “substantially equivalent” to an existing, approved device (Hines et al., 2010).

Very few double-blind RCTs have been conducted on CES as a treatment for MDD, and the majority of the existing trials suffer from methodological shortcomings, including failure to use standardized diagnostic criteria to diagnose depression, lack of a sham comparator condition, or compromised blinding due to the sham CES not producing a local tingling sensation (Kavirajan et al., 2014). The two recent trials highlighted above mark an improvement in the methodology from previous trials, but are not generalizable to a population of adults with MDD, and still suffer from inadequate sample sizes and compromised blinding. The current state of the CES evidence base is not mature enough to recommend CES as an evidence-based treatment for use during a major depressive episode in patients with MDD in the MHS.

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## **References**

- Barclay, T. H., & Barclay, R. D. (2014). A clinical trial of cranial electrotherapy stimulation for anxiety and comorbid depression. *J Affect Disord*, 164, 171–177.
- Department of Veterans Affairs/Department of Defense. (2016). VA/DoD clinical practice guideline for management of major depressive disorder. Version 3.0. Washington (DC): Department of Veterans Affairs/Department of Defense.
- Gaynes, B. N., Lux, L. J., Lloyd, S. W., Hansen, R. A., Gartlehner, G., . . . Lohr, K. N. (2011). Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults. Comparative Effectiveness Review No. 33. (AHRQ Publication No. 11-EHC056-EF). Rockville, MD: Agency for Healthcare Research and Quality.
- Hines, J. Z., Lurie, P., Yu, E., Wolfe, S. Left to their own devices: breakdowns in the United States medical device premarket review. *PLOS Medicine* 2010;7(7):e1000280.
- Kavirajan, H. C., Lueck, K., & Chuang, K. (2014). Alternating Current Cranial Electrotherapy Stimulation (CES) for Depression. *Cochrane Database Syst Rev*, 7, CD010521.
- Mischoulon, D., De Jong, M. F., Vitolo, O. V., Cusin, C., Dording, C. M., Yeung, A. S., . . . Dougherty, D. D. (2015). Efficacy and safety of a form of cranial electrical stimulation (CES) as an add-on intervention for treatment-resistant major depressive disorder: A three week double blind pilot study. *J Psychiatr Res*, 70, 98–105.
- Rosa, M. A., & Lisanby, S. H. (2012). Somatic Treatments for Mood Disorders. *Neuropsychopharmacology*, 37(1), 102–116.

