

The following studies, dating back to 1983, meet the FDA criteria of "valid scientific evidence" (21 CFR 860.7) for safety and effectiveness. When "taken as a whole" this evidence clearly provides reasonable assurance of the safety and effectiveness of Alpha-Stim CES to any non biased reviewer.

The "well controlled investigations" according to the FDA's definition in 21 CFR 860.7(e)(2) are 1-21 (all the RCTs), 34, 35, 37, 39, 40, 41 and 42.

Although some of these studies used Alpha-Stim CES for pain or attention or other indications, most of those included an evaluation of anxiety, insomnia and or depression and the balance of these studies contribute to the general fund of data on safety of Alpha-Stim CES technology.

Many more studies (12) being financed and conducted by the United States government are underway now by the NIH, NCI and within the department of defense, veterans affairs medical centers as well as several universities within and outside of the USA.

Randomized Controlled Trials

1. Taylor, Ann G., Anderson, Joel G., Riedel, Shannon R., Lewis, Janet E., Kinser, Patricia A. and Bourguignon, Cheryl. Cranial electrical stimulation improves symptoms and functional status in individuals with fibromyalgia. *In Progress* 2012.
2. US GOVERNMENT FINANCED AND US GOVERNMENT CONDUCTED STUDY. Tan, Gabriel, Rintala, Diana, Jensen, Mark P., Richards, J. Scott, Holmes, Sally Ann, Parachuri, Rama, Lashgari-Saegh, Shamsi and Price, Larry R. Efficacy of cranial electrotherapy stimulation for neuropathic pain following spinal cord injury: a multi-site randomized controlled trial with a secondary 6-month open-label phase. *The Journal of Spinal Cord Medicine*, 34(3):285-296, 2011.
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5. Strentzsch, Julie A. An examination of cranial electrotherapy stimulation (CES) on alpha-amylase levels, cortisol levels and state-trait anxiety scores in the chronically mentally ill. Doctoral dissertation, Saint Mary's University, San Antonio, Texas. 121 pages, 2008. Poster Presentation at the International Society of Neurotherapy and Research 17th Annual Conference, Indianapolis, Indiana, September 4, 2009.
6. STATE GOVERNMENT FINANCED AND STATE GOVERNMENT CONDUCTED STUDY. Mellen, Ronald R. and Mackey, Wade. Reducing sheriff's officers' symptoms of depression using cranial electrotherapy stimulation (CES): a control experimental study. *The Correctional Psychologist*, 41(1):9-15, 2009.
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9. US GOVERNMENT FINANCED AND US GOVERNMENT CONDUCTED STUDY. Tan, Gabriel, Rintala, Diana H., Thornby, John, Yang, June, Wade, Walter, and Vasilev, Christine. Using cranial electrotherapy stimulation to treat pain associated with spinal cord injury. *Journal of Rehabilitation Research and Development*, 43(4):461-474, 2006.
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12. Schroeder, M.J., and Barr, R.E. Quantitative analysis of electroencephalogram during cranial electrotherapy stimulation. *Clinical Neurophysiology*. 112:2075-2083, 2001. Doctoral dissertation, The Graduate School of the University of Texas at Austin, 191 pages, 1999.
13. Winick, Reid L. Cranial electrotherapy stimulation (CES): a safe and effective low cost means of anxiety control in a dental practice. *General Dentistry*, 47(1):50-55,1999.
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Open Clinical Trials

22. Raines, Christopher K., Stevens, Emily, Manners, Keaton R., Mottashed, Sarah, Malone, Melissa. The use of CES to reduce anger and anxiety in pediatric patients. *In Progress* 2012.
23. US GOVERNMENT FINANCED AND US GOVERNMENT CONDUCTED STUDY. Tan, Gabriel, Dao, Tam K., Smith, Donna L., Robinson, Andrew and Jensen, Mark P. Incorporating Complementary and Alternative Medicine (CAM) Therapies to Expand Psychological Services to Veterans Suffering From Chronic Pain. *Psychological Services*, 7(3):148-161, 2010.
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Case Series and Case Reports

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31. Annibali, Joseph. Case of the Week: Jeff – Bipolar Disorder and More. Published online at [http: www.amenclinics.com](http://www.amenclinics.com) blog tag alpha-stim-100, April 22, 2010.
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Mechanistic Studies

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