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Prospective Study of Brain Wave Changes Associated With Cranial Electrotherapy Stimulation

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ABSTRACT

Objective: To explore brain wave changes associated with cranial electrotherapy stimulation (CES) among subjects receiving psychiatric care.

Methods: Quantitative electroencephalogram data were obtained before and after a 20-minute session of CES. The investigators recruited active-duty military subjects from Walter Reed National Military Medical Center's Psychiatry Continuity Service, Bethesda, Maryland. Fifty subjects participated in this prospective, convenience sample study from August 2016 through March 2017. The main outcome measures were changes in brain wave activity and the Subjective Units of Distress Scale.

Results: The typical subject was mildly depressed and had severe trauma-related symptoms and sleep problems. There was a significant increase ($P = .000$) in the higher beta frequencies (18–21 Hz, 21–33 Hz, and 33–48 Hz) and a strong effect (with the Cohen d around 1.5) immediately following the 20-minute CES. Ten minutes after CES, slower wave activity (4–8 Hz and 8–12 Hz) significantly decreased ($P < .05$), while higher beta wave activity (13–15 Hz, 18–21 Hz, and 21–33 Hz) increased. A strong effect (with the Cohen d around 1.5) persisted in the beta brain wave bands 18–21 Hz and 21–33 Hz.

Conclusions: Brain wave measurements taken immediately after the 20-minute CES session showed a significant and strong effect in the beta region, suggesting an increase in mental alertness, focus, and concentration. Ten minutes after the CES session, an even more marked change in brain wave activity occurred. The significant and strong effect in the beta region persisted but was joined by a reduction in slower wave activity, indicating an increase in mental alertness.

Trial Registration: ClinicalTrials.gov identifier NCT03298308

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Cranial electrotherapy stimulation (CES) is a noninvasive intervention marketed by manufacturers for the treatment of pain, insomnia, and emotional disorders such as depression and anxiety. Devices differ in terms of such fundamental variables as electrode placement, frequency ranges, and stimulation patterns, all of which compound the difficulties researchers confront when investigating the efficacy of CES. Despite these obstacles, investigators continue efforts to examine the efficacy and putative mechanism of actions for CES as a nonpharmacologic treatment.¹

As a potential therapeutic modality, CES relies in part on a long history of clinicians using both electricity and magnets for various medical treatments. Modern examples include electroconvulsive therapy, transcranial magnetic stimulation, and deep-brain stimulation, all of which are best reserved for individuals with treatment-resistant depression and other severe, chronic psychiatric disorders.^{2–4} Efficacy aside, these treatments have significant limitations in terms of cost, training, and side effects, which are major obstacles to widespread availability.⁵

CES is microcurrent therapy: a less intensive version of transcranial electrical stimulation, requiring less training and exposing the recipient to fewer side effects. Modern CES can trace its development to the 1970s when early efforts to standardize the procedure resulted in 2 earlobe-attached electrodes, the delivery of microamperage, and a 20-minute treatment duration. The combination of electrodes and their placement, amount of microamperage, waveform characteristics, duration of exposure, and type of stimulation together constitute the definition of a CES dose. In 1979, the US Food and Drug Administration recognized CES as class III devices for the treatment of anxiety, depression, and insomnia. Since that time, manufacturers have brought new devices to the commercial market with different dosing criteria.⁶

Dosing parameters are critical variables in determining the potential value of CES. Perhaps the most fundamental issue is whether ear electrode placement and pulsed microcurrent stimulation actually penetrate the skull and reach deeper-lying brain regions; a question affirmatively answered through a computer-based modeling study.⁷

A review⁸ of published literature cited improvement in anxiety, depression, and insomnia as the result of microcurrent-induced changes in the neurophysiology of the brain. Researchers reported the effectiveness of CES for anxiety, depression, and insomnia through randomized, double-blind, sham-controlled designs.^{9–11}

Aside from possible changes in CES-induced neurotransmitter levels, another line of inquiry explored by investigators and the subject of this research involves variations in brain wave activity as a consequence of the microcurrents. Among presumably healthy volunteers, a 20-minute session of CES resulted in an

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- Cranial electrotherapy stimulation (CES) is easily administered in the typical office or hospital setting.
- CES is a nonpharmacologic treatment alternative—an option to consider when other approaches have not achieved optimum results.
- On the basis of the study findings, CES may improve concentration and reduce distractibility.

increase in alpha wave activity and decreased delta and theta waves with subjective reports of mental clarity.¹² In another small study¹³ of healthy individuals, investigators reported a decrease in the alpha brain wave's median frequency and the beta brain wave's power band.

In this study, we examined brain wave changes associated with CES among subjects receiving psychiatric care. We hypothesized that CES would decrease subjective reports of anxiety by increasing alpha wave activity or paradoxically be interpreted as anxiolytic by an increase in beta wave activity, favorably improving concentration, focus, and mental acuity. Walter Reed National Military Medical Center's Institutional Review Board approved this prospective study. Trial registration information is available from ClinicalTrials.gov (identifier NCT03298308).

METHODS

This study was conducted from August 2016 through March 2017 among active-duty service members receiving treatment at the Psychiatry Continuity Service, Walter Reed National Military Medical Center in Bethesda, Maryland. The Psychiatry Continuity Service is an outpatient partial hospital program staffed by a group of multidisciplinary clinicians and provides intensive care for all psychiatric disorders requiring this level of treatment.¹⁴

Subjects supplied quantitative electroencephalogram (qEEG) data using the NeuroSky MindSet (San Jose, California), a wireless single-channel dry electrode device processing research-grade electrical activity from the Fp1 (frontal scalp, position 1 location).¹⁵ NeuroSky's ThinkGear ASIC Module processes the brain's electrical activity and reports EEG values and signal quality.^{16,17} Its qEEG data acquisition offers convenience, reliability, and reproducibility.¹⁸

The investigators analyzed the qEEG data using the SmartMind Research Kit (BrainTrain, North Chesterfield, Virginia), which incorporates software bandpass filters and minimizes artifacts from eye and muscle movement. SmartMind reports the mean and standard deviation in microvolts for each sampled brain wave frequency for a user-defined period of time.^{19,20}

Subjects received CES from the Alpha-Stim AID (Electromedical Products International, Mineral Wells, Texas). Through ear clip electrodes, the Alpha-Stim AID delivers 0–500 microamperes adjustable in 50-microampere increments at a frequency of 0.5 Hz (pulses per second)

Table 1. Self-Test Scores for 50 Subjects

Test	Mean	SD
AUDIT	4.3	5.1
SDS	45.7	9.9
SAS	37.7	12.6
PCL-5	46.8	20.7
PIRS	38.0	12.4

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, PCL-5 = PTSD Checklist for DSM-5, PIRS = Pittsburgh Insomnia Rating Scale, SAS = Zung Self-rating Anxiety Scale, SDS = Zung Self-rating Depression Scale.

combined with a constant 0.4 Hz, producing a mean pulse repetition frequency rate of 0.8 Hz, with bipolar asymmetric rectangular waves at a 50% duty cycle repeating periodically at 10-second intervals.²¹

Subjects received an orientation on use of the equipment after providing written consent. The subjects placed the qEEG device on their head with their eyes open and their head resting against a wall in a quiet room for the duration of the experiment. An investigator assured proper positioning of the CES ear clips and then adjusted the microamperage to the point of mild subjective discomfort, then reduced the microamperage to eliminate that sensation, which replicates the process performed in clinical practice. Subjects received CES for 20 minutes. We recorded 30-second measurements of brain wave activity at baseline immediately preceding CES, immediately after the 20-minute CES, and 10 minutes after CES.

In addition to the brain wave measurements, just before and after CES, study participants completed the Subjective Units of Distress Scale.²² Baseline self-assessment instruments included the Alcohol Use Disorders Identification Test (AUDIT),²³ PTSD Checklist for DSM-5 (PCL-5),²⁴ Pittsburgh Insomnia Rating Scale (PIRS),²⁵ Zung Self-rating Anxiety Scale (SAS),²⁶ and Zung Self-rating Depression Scale (SDS).²⁷ For purposes of screening clinical conditions, the following thresholds apply: AUDIT ≥ 8 , PCL-5 ≥ 33 , PIRS ≥ 21 , SAS ≥ 45 , and SDS ≥ 45 .

Data were studied through correlations, independent samples *t* test, paired samples *t* test, frequencies, and descriptive analyses using SPSS version 22.

RESULTS

Fifty subjects participated in this study; most were male ($n = 34/50$, 68%), enlisted service members ($n = 39/50$, 78%) between the ages of 21 and 40 years ($n = 37/50$, 74%). The typical subject was mildly depressed and had severe trauma-related symptoms and sleep problems (Table 1).

There was a significant difference in the subjective units of distress before CES ($n = 50$, mean = 4.12, SD = 2.12) and after CES ($n = 50$, mean = 3.26, SD = 2.19, $P = .000$, Cohen $d = 0.4$). Microamperage during CES ranged between 0.5 and 5.0 ($n = 50$, mean = 3.28, SD = 0.98).

In terms of brain wave changes, there was a significant increase ($P = .000$) in the higher beta frequencies (18–21

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Table 2. Changes in Brain Wave Activity in 50 Subjects After 20-Minute Cranial Electrotherapy Stimulation (CES-20) and 10 Minutes After Stimulation (CES-10)^a

Frequency	Mean	SD	P Value	Cohen <i>d</i>
0.5–3.5 Hz				
Baseline	9.67	6.13		
CES-20	13.25	7.73	.007**	0.51
CES-10	10.38	6.74	.545	0.11
4–8 Hz				
Baseline	10.75	5.44		
CES-20	11.81	6.32	.337	0.18
CES-10	8.64	3.81	.014**	0.45
8–12 Hz				
Baseline	6.75	2.67		
CES-20	7.49	4.01	.226	0.22
CES-10	5.97	2.37	.049*	0.31
13–15 Hz				
Baseline	4.86	2.44		
CES-20	5.34	3.13	.279	0.17
CES-10	5.97	2.37	.002**	0.46
15–18 Hz				
Baseline	5.11	2.79		
CES-20	4.90	2.93	.663	0.08
CES-10	3.86	1.91	.001**	0.52
18–21 Hz				
Baseline	1.81	0.74		
CES-20	4.45	2.30	.000**	1.55
CES-10	3.89	1.70	.000**	1.59
21–33 Hz				
Baseline	3.65	1.97		
CES-20	8.76	4.47	.000**	1.48
CES-10	8.23	4.08	.000**	1.43
33–48 Hz				
Baseline	3.12	1.63		
CES-20	7.34	3.71	.000**	1.47
CES-10	2.95	1.13	.387	0.12

^aStatistics are in comparison with baseline. *P* values are 2-tailed.

P* < .05. *P* < .01.

Hz, 21–33 Hz, and 33–48 Hz) and a strong effect (with the Cohen *d* around 1.5) immediately following the 20-minute CES (Table 2).

Ten minutes after CES, slower wave activity (4–8 Hz and 8–12 Hz) significantly decreased, while higher beta wave activity (13–15 Hz, 18–21 Hz, and 21–33 Hz) increased. A strong effect (with the Cohen *d* around 1.5) persisted in the beta brain wave bands 18–21 Hz and 21–33 Hz (Table 2).

There was a direct correlation between the amount of microamperage delivered and brain wave activity between 13–15 Hz (*n* = 50, *r* = 0.27, *P* = .05) and 18–21 Hz (*n* = 50, *r* = 0.33, *P* = .02). Age and sex did not correlate with any brain wave changes.

DISCUSSION

We explored acute brain wave changes associated with CES in a manner specifically designed to reduce external variables that might affect the results. At the same time, subjects received CES with the microamperage adjusted as in clinical practice. In sham-controlled studies,¹⁰ the electrical current is not adjusted, leaving the clinical relevance of this approach unanswered. Findings from this study would suggest that variations in the microamperage predominately affect midrange beta waves.

Brain wave activity was grouped into 5 categories on the basis of their respective frequencies: alpha (8–12 Hz), theta (4–8 Hz), beta (13–15 Hz, 15–18 Hz, 18–21 Hz, and 21–33 Hz), delta (0–3.5 Hz), and gamma (33–48 Hz). Alpha waves correlate with a relaxed mental state, theta waves correlate with drowsiness, beta waves correlate with increased attention and cognition, delta waves may occur while awake but are more prominent in deep sleep, and gamma waves correlate with global consciousness and synchronized neuronal activity.^{28,29} The frequency range of 13–15 Hz is a transition phase with functional elements of both mental tranquility and alertness, which overlaps slightly with the next frequency range.³⁰ The progression from the slow-frequency delta waves to the high-frequency gamma waves represents increasing levels of mental acuity in the broadest and simplest description of functional activity.

Brain wave measurements taken immediately after the 20-minute CES session showed a significant increase and strong effect size in the beta region, suggesting an increase in mental alertness, focus, and concentration.

An even more marked change in brain wave activity occurred 10 minutes after the CES session. The significant increase and strong effect size in the beta region persisted but was joined by a reduction in slower wave activity, indicating an increase in mental alertness.

Participants in this study subjectively reported a significant reduction in distress following the CES session. This finding raises the possibility that the subjective assessment of stress reduction following CES may be related to an increase in beta wave activity. Improved mental focus and a corresponding decrease in distraction may be a welcome relief among individuals with overlapping anxiety, depression, and trauma symptoms as reflected in this study group.

This study was designed to balance the actual clinical use of CES with scientific rigor. As in clinical practice, the microamperage of CES was tailored for each subject. On the other hand, to minimize distractions we conducted the study in a quiet office, specifically limited all communication, required that the subjects keep their eyes open, and minimized the time span between qEEG measurements in an effort to avoid other confounding variables affecting brain wave activity.

We acknowledge that balancing clinical use and scientific rigor is not perfect. This open-label study exposed the subjects to limited interactions, such as positioning the brain wave-sensing headset, with the investigators. While other factors such as the subjects' awareness of the stimulation phase of CES may impose a potential bias on the study's results, it is at least partially mitigated by the number of subjects, the strength of the findings, and the value in determining the role of microamperage dosing.

With these limitations in mind, the findings of this study would benefit from replication with a larger study group among subjects with similar behavioral profiles. Future research could also further explore the anxiolytic effects of increasing beta wave activity among individuals with varying degrees of mental distraction.

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