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Cranial Electrotherapy Stimulation for Fibromyalgia Pain and Function in Veterans

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Introduction

Cranial electrotherapy stimulation (CES) is a non-invasive, FDA-cleared therapy for the treatment of insomnia, anxiety, depression, and pain. We present an analysis of a randomized, double-blind, sham-controlled trial using CES transcranial alternating current stimulation (tACS) to determine the impact on pain, function, sleep, mood, and global health of veterans with fibromyalgia. We further tested the utility of resting state functional connectivity magnetic imaging (rs-fcMRI) as a novel biomarker for pain using a seed-to-voxel analysis comparing post-baseline rs-fcMRI scans of those who received the True CES device and those who received the Sham.

Materials and Methods

This is an analysis of 33 veterans with FM who were randomized to sham (n=17) or true (n=16) CES. Pain, assessed with the Defense and Veterans Pain Rating Scale (DVPRS), physical function outcomes, PROMIS measures related to pain and function, and rs-fcMRI data were collected at baseline, 6 weeks, and 12 weeks following daily CES treatment. Participants and staff were blinded until all study visits were completed. A 2-groups (true vs. sham) x 3 times (pre- and post- treatment at 6- and 12-weeks follow-up) analysis of the variance was used to compare outcomes for the groups over time. Linear mixed effects modeling was used to fit the ANOVA model to the data. Neuroimaging data was analyzed using the CONN toolbox in 32 participants (True=16, Sham=16). This study was approved by the Institutional Review Board of Emory University (IRB00112768).

Results/Case Report

All participants experienced statistically significant reductions in DVPRS at 12 weeks (-1.65, 95% CI: (-2.29, -1.01), $p<0.01$), and reductions in pain interference with activity (-1.83, 95% CI: -2.52, -1.15, $p<0.01$), sleep (-2.25, 95% CI: (-3.06, -1.43), $p<0.01$), mood (-1.88, 95% CI: (-2.62, -1.15), $p<0.01$), and stress (-1.77, 95% CI: (-2.67, -0.89), $p<0.01$) at 12 weeks. No statistically significant differences were found between CES and Sham groups in our initial intent-to-treat analysis, however a per protocol analysis is pending.

In True CES compared to Sham, from baseline to post-treatment, rs-fcMRI revealed significantly increased functional connectivity (FC) from the right cerebellar 7b seed to the left fusiform gyrus, lingual gyrus, left occipital pole and left temporal occipital fusiform cortex.

Discussion

All participants experienced improvements in pain intensity and interference. This 2-point reduction in pain score is clinically meaningful and may suggest a meditative effect of the daily prescribed protocol, as all participants were asked to wear the device and sit daily for 60 minutes, and meditation interventions have shown promise for improvement of pain in fibromyalgia.[1,2]

The neuroimaging outcomes revealed enhanced connectivity between the cerebellar seed and regions implicated in visual processing and memory. The cerebellum has been increasingly recognized for its involvement in pain processing, and the cerebellar lobule 7b plays a significant role in different dimensions of pain perception.[3,4] The observed connectivity underscores this multimodal processing and suggests an interplay between the cerebellum and sensory and cognitive regions that CES may influence.[4,5] This study address the need for non-pharmacologic chronic pain management strategies and an understanding of their neural underpinnings.

References

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Disclosures
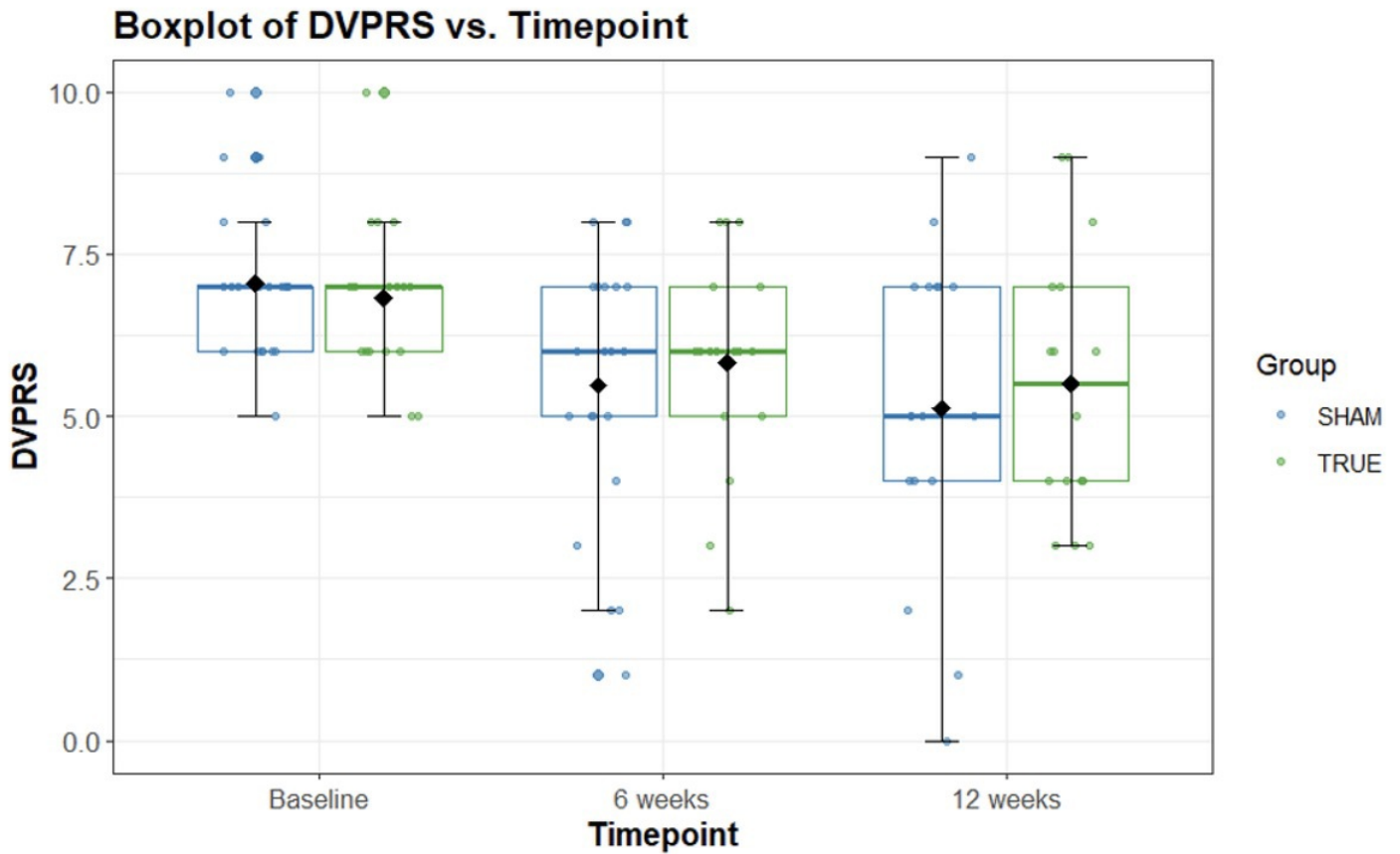
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Tables / Images

Boxplot of DVPRS vs. Timepoint

Figure 1: Boxplot of DVPRS at baseline, 6 weeks, and 12 weeks in CES (True) and Sham groups. Subjects are denoted by dots, center line denotes median value, diamond represents mean, bounds of box denotes interquartile range, and whiskers represent range of bulk data with outliers represented as distinct points outside of whiskers.
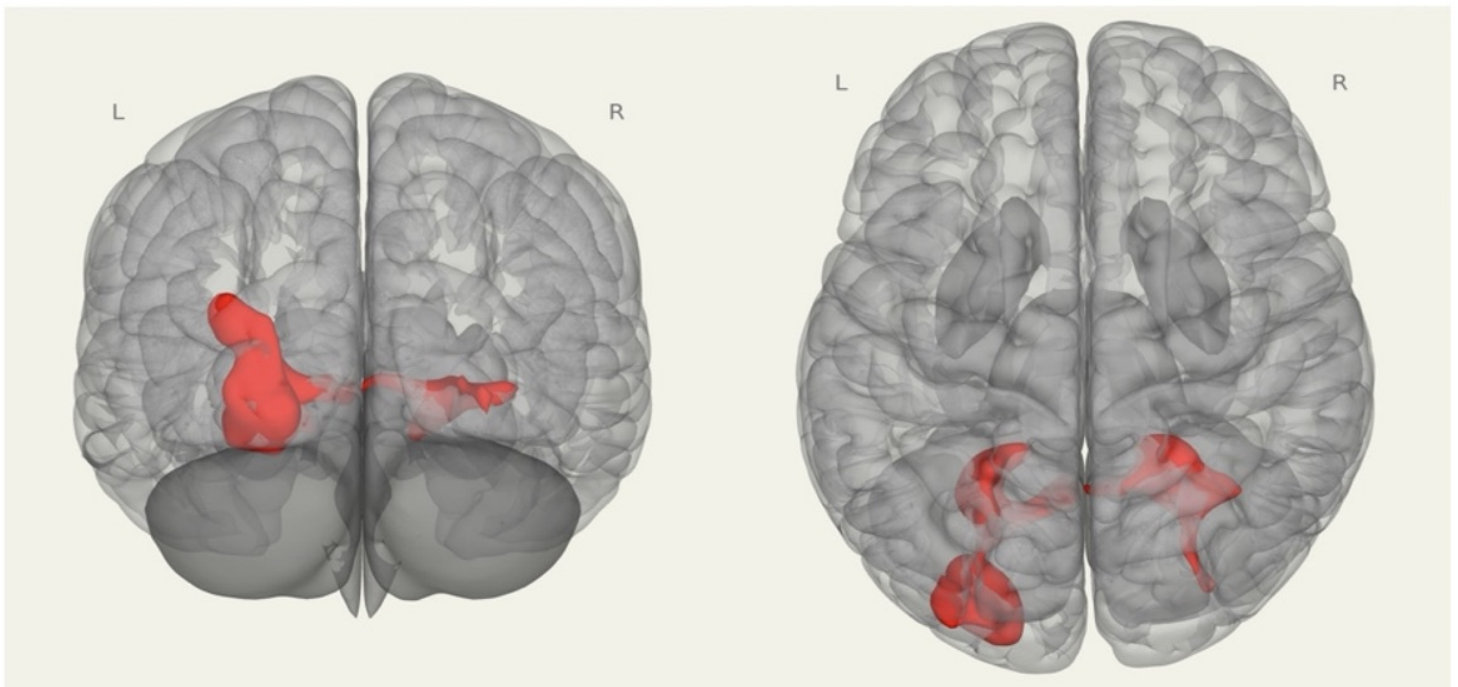

Figure 2: Seed-based connectivity analysis using cerebellar 7b seed. Highlighted regions represent increased functional connectivity in True CES group compared to the Sham group from baseline to post-treatment (voxel threshold, p<.005, cluster threshold, p<.0016, family wise error-corrected (FWE-c)).

Table 1: Demographic and characteristics of participants at baseline, by treatment group

	SHAM (N=17)	TRUE (N=16)	Overall (N=33)
Age	48.9 (7.87)	50.3 (7.03)	49.6 (7.39)
Sex			
Female	12 (70.6%)	10 (62.5%)	22 (66.7%)
Male	5 (29.4%)	6 (37.5%)	11 (33.3%)
Race			
African American	10 (58.8%)	12 (75.0%)	22 (66.7%)
White	7 (41.2%)	4 (25.0%)	11 (33.3%)
DVPRS	7.06 (1.30)	6.75 (1.24)	6.91 (1.26)
WPI	13.3 (3.20)	12.4 (3.44)	12.8 (3.30)
SSS	8.94 (2.16)	8.69 (1.66)	8.82 (1.91)

Data are N(%) or Mean (SD); DVPRS: Defense and Veterans Pain Rating Scale; WPI: Widespread Pain Index; SSS: Symptom Severity Score