Effects of Cranial Electrical Stimulation on Activity in Regions of the Basal Ganglia in Individuals with Fibromyalgia

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Fibromyalgia (FM) is a chronic syndrome characterized by widespread pain that affects up to 4% of the U.S. population.1 Neuroimaging studies suggest FM may be linked to dysregulation of brain activity.23 However, the cross-sectional nature of these findings do not address whether this dysregulation is the cause or consequence of pain and symptoms of FM, or of chronic pain generally.

On the basis of evidence that brain processing of pain is disturbed in FM, treatment with actions targeted toward the brain should be particularly promising. Over the years, several types of electrical stimulation of the brain have been used to reduce pain or depression.4 One such device, Alpha-Stim (Electromedical Products International, Inc., Mineral Wells, TX), is a Food and Drug Administration (FDA)–approved (FDA K903014) medical device for pain relief, suitable for at-home use.

The effects of cranial electrotherapy stimulation (CES) are believed to be primarily mediated through direct action on the brain, likely at the limbic system, hypothalamus, thalamus, or reticular activating system.5 However, few data exist on the potential neural correlates of mechanisms by which CES may affect pain in general or, more specifically, in those with FM. Thus, the goal of the current study was to examine the effects of CES therapy using a double-blind, randomized, controlled design to collect functional magnetic resonance imaging (fMRI) data on activation in brain regions.

Potential participants were recruited as part of a larger study6,7 and remained on their usual care regimen during the study. Participants were assigned randomly to one of three groups: usual care alone, usual care plus a sham CES device, or usual care plus an active CES device. Participants in the two device groups were instructed to use the Alpha-Stim CES device for 60 continuous minutes each day for 8 weeks. Participants in the active CES device group received devices that were preset to provide a modified square-wave biphasic stimulation below the level of perception. Participants in the sham device group received devices that appeared to be activated but did not deliver any stimulation.

A subset of participants in each of the two device groups (active CES, n = 6; sham CES, n = 6) underwent fMRI at baseline and week 8 to measure brain activation at rest and during a pain stimulation procedure. Motion-corrected functional data (Digital Imaging and Communications in Medicine format) for each patient were loaded into BrainVoyager QX (Brain Innovations, Maastricht, the Netherlands) for pre-processing and converted to BrainVoyager’s internal data format for analysis as previously described.7 Regions of interest, both a priori and a posteriori, were identified by using areas of the brain in which changes in blood oxygen level dependence (BOLD) were significantly different from baseline to week 8 between the two device groups.

As previously reported, persons using the active device had a greater decrease in average pain, fatigue, and sleep disturbance and an improvement in functional status over time than those using the sham device or usual care alone (p < 0.05).6 Preliminary analyses of fMRI data showed that persons using an active CES device had decreased activation of pain-processing regions of the brain compared with those using a sham device.7 In addition to changes in regions of the brain reported previously, decreased activity was observed in the basal ganglia (caudate, putamen, and globus pallidus) and parahippocampal gyrus in individuals using the active CES versus the sham device (p < 0.05).

Recently, the role of the basal ganglia in pain perception has been revealed. Increased neural activity as evidenced by fMRI has been shown in the basal ganglia in persons with FM.8 Additional findings indicate a role for the basal ganglia in pain suppression with regard to dopamine receptors, which may be impaired in patients with FM.9 In the current study, the decreased activity observed in the basal ganglia of the active CES device group may be related to the decreased pain observed over time in these persons. Moreover, differences in regional brain activity in the basal ganglia may affect other symptoms of FM affected by CES use, particularly the observed decrease in fatigue. Patients with multiple sclerosis who experience chronic fatigue displayed increased activation in the basal ganglia,9 while persons diagnosed with chronic fatigue demonstrated increased activation in the parahippocampal gyrus,10 regions that displayed decreased activity in response to active CES in the current study.

As increasing evidence points toward dysregulation of neural networks in the pathophysiology of FM, neuroimaging...
may enhance the characterization of this disease state and track changes in symptoms over time in this patient population, as well as provide data to support the use of non-pharmacologic interventions.

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References


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